SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 20-F

☐ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

Or

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2014

Or

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Or

☐ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission File No. 001-36203

CAN-FITE BIOPHARMA LTD.

(Exact name of Registrant as specified in its charter)

Can-FiteBioPharma Ltd., an Israeli Limited Company
(Translation of the Registrant's name into English)

Israel
(Jurisdiction of incorporation)

10 Bareket Street, KiryatMatalon, P.O. Box 7537, Petah-Tikva 4951778, Israel
(Address of principal executive offices)

Motti Farbstein
Chief Operating and Financial Officer
Tel: +972 (3) 924-1114
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10 Bareket Street, KiryatMatalon, P.O. Box 7537, Petah-Tikva 4951778, Israel
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

American Depositary Shares, each representing 2 Ordinary Shares, par value NIS 0.25 per share
(Title of Class)

Ordinary Shares, par value NIS 0.25 per share*
(Title of Class)

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

* Not for trading, but only in connection with the registration of the American Depositary Shares.

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report (December 31, 2014): 21,316,577 are issued and outstanding, (excluding 446,827 ordinary shares held as treasury shares).

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such a shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☐ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one): Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ☒	Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the Registrant has elected to follow: Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

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USE OF CERTAIN TERMS

In this Annual Report on Form 20-F, unless the context otherwise requires:

- references to "ADSs" refer to the Registrant's American Depositary Shares;
- references to "A3AR" refer to the A3 adenosine receptor;
- references to the "Company," "we," "our" and "Can-fite" refer to Can-fiteBioPharma Ltd. (the "Registrant") and its consolidated subsidiaries;
- references to the "Companies Law" or "Israeli Companies Law" are to Israel's Companies Law, 5759-1999, as amended;
- references to "dollars," "U.S. dollars" and "$" are to United States Dollars;
- references to "HCC" refer to hepatocellular carcinoma, also known as primary liver cancer;
- references to "HCV" refer to hepatitis C virus;
- references to "ordinary shares," "our shares" and similar expressions refer to the Registrant's Ordinary Shares, NIS 0.25 nominal (par) value per share;
- references to "OA" refer to osteoarthritis;
- references to "PBMC" refer to peripheral blood mononuclear cells;
- references to "RA" refer to rheumatoid arthritis;
- references to "Securities Law" or "Israeli Securities Law" are to Israel Securities Law, 5728-1968, as amended;
- references to "shekels" and "NIS" are to New Israeli Shekels, the Israeli currency; and
- references to the "SEC" are to the United States Securities and Exchange Commission.

FORWARD LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements, about our expectations, beliefs or intentions regarding, among other things, our product development efforts, business, financial condition, results of operations, strategies or prospects. In addition, from time to time, we or our representatives have made or may make forward-looking statements, orally or in writing. Forward-looking statements can be identified by the use of forward-looking words such as "believe," "expect," "intend," "plan," "may," "should" or "anticipate" or their negatives or other variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical or current matters. These forward-looking statements may be included in, but are not limited to, various filings made by us with the U.S. Securities and Exchange Commission, or the SEC, press releases or oral statements made by or with the approval of one of our authorized executive officers. Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements, including, but not limited to, the factors summarized below.

This Annual Report on Form 20-F identifies important factors which could cause our actual results to differ materially from those indicated by the forward-looking statements, particularly those set forth under the heading "Risk Factors." The risk factors included in this Annual Report on Form 20-F are not necessarily all of the important factors that could cause actual results to differ materially from those expressed in any of our forward-looking statements. Given these uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. Factors that could cause our actual results to differ materially from those expressed or implied in such forward-looking statements include, but are not limited to:

- the initiation, timing, progress and results of our preclinical studies, clinical trials and other product candidate development efforts;
- our ability to advance our product candidates into clinical trials or to successfully complete our preclinical studies or clinical trials;
- our receipt of regulatory approvals for our product candidates, and the timing of other regulatory filings and approvals;
- the clinical development, commercialization and market acceptance of our product candidates;
- our ability to establish and maintain corporate collaborations;
- the implementation of our business model and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- competitive companies, technologies and our industry; and
- statements as to the impact of the political and security situation in Israel on our business.

All forward-looking statements attributable to us or persons acting on our behalf speak only as of the date of this Annual Report on Form 20-F and are expressly qualified in their entirety by the cautionary statements included in this Annual Report on Form 20-F. We undertake no obligations to update or revise forward-looking statements to reflect events or circumstances that arise after the date made or to reflect the occurrence of unanticipated events. In evaluating forward-looking statements, you should consider these risks and uncertainties.

EXPLANATORY NOTE

Market data and certain industry data and forecasts used throughout this Annual Report on Form 20-F were obtained from internal company surveys, market research, consultant surveys, publicly available information, reports of governmental agencies and industry publications and surveys. Industry surveys, publications, consultant surveys and forecasts generally state that the information contained therein has been obtained from sources believed to be reliable, but that the accuracy and completeness of such information is not guaranteed. We have not independently verified any of the data from third-party sources, nor have we ascertained the underlying economic assumptions relied upon therein. Similarly, internal surveys, industry forecasts and market research, which we believe to be reliable based upon our management's knowledge of the industry, have not been independently verified. Forecasts are particularly likely to be inaccurate, especially over long periods of time. In addition, we do not necessarily know what assumptions regarding general economic growth were used in preparing the forecasts we cite. Statements as to our market position are based on the most currently available data. While we are not aware of any misstatements regarding the industry data presented in this Annual Report on Form 20-F, our estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" in this Annual Report on Form 20-F.

We effected a 1-for-25 reverse share split with respect to our ordinary shares, options and warrants on May 12, 2013. Unless indicated otherwise by the context, all ordinary share, option, warrant and per share amounts as well as stock prices appearing in this annual report have been adjusted to give retroactive effect to the share split for all periods presented.

PART I

ITEM 1. Identity of Directors, Senior Management and Advisers.

Not applicable.

ITEM 2. Offer Statistics and Expected Timetable.

Not applicable.

ITEM 3. Key Information.

A. Selected Financial Data.

The following table sets forth our selected consolidated financial data for the periods ended and as of the dates indicated. The following selected consolidated financial data for our company should be read in conjunction with the financial information, "Item 5. Operational and Financial Review and Prospects" and other information provided elsewhere in this Annual Report on Form 20-F and our consolidated financial statements and related notes. The selected consolidated financial data in this section is not intended to replace the consolidated financial statements and is qualified in its entirety thereby.

The selected consolidated statements of operations data for the years ended December 31, 2014, 2013 and 2012, and the selected consolidated balance sheet data as of December 31, 2014 and 2013, have been derived from our audited consolidated financial statements set forth elsewhere in this Annual Report on Form 20-F. The selected consolidated statements of operations data for the years ended December 31, 2011 and 2010, and the selected consolidated balance sheet data as of December 31, 2012, 2011 and 2010, have been derived from our audited consolidated financial statements not included in this Form 20-F.

Our consolidated financial statements included in this Annual Report on Form 20-F were prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, and reported in Israeli New Shekels, or NIS.

Consolidated Statements Of Operations Data:	**Year Ended December 31,**					
	2010	**2011**	**2012**	**2013**	**2014**	**2014**
	(in thousands, except share and per share data)					
	NIS				Convenience translation to US $	
Revenues	2,644	1,785	-	-	-	-
Operating expenses:						
Research and development, expenses net	9,993	12,969	13,160	15,390	16,200	4,165
General and administrative expenses	6,005	6,934	9,272	15,922	11,573	2,976
Operating loss	13,354	18,118	22,432	31,312	27,773	7,141
Other expense – due to M&A	-	11,496	-	-	-	-
Financial expenses	356	232	59	892	1,228	316
Financial income	(897)	(1,669)	(573)	(1401)	(4,500)	(1,157)
Taxes on income	235	191	11	9	23	6
Net loss	13,048	28,368	21,929	30,812	24,524	6,306
Adjustments arising from translating financial statements of foreign operations	-	(92)	(7)	206	939	241
Remeasurments of defined benefit plan	-	59	(42)	49	94	24
Comprehensive loss	13,048	28,335	21,880	31,067	25, 557	6,571
Net loss per ordinary share	1.50	2.72	2.08	2.12	1.35	0.35
Number of ordinary shares used in computing loss per ordinary share	8,687,311	9,708,505	10,050,927	13,712,521	17,545,663	17,545,663

Consolidated Balance Sheet Data:	As of December 31,					
	2010	2011	2012	2013	2014	2014
	(in thousands NIS)	(in thousands NIS)	(in thousands NIS)	(in thousands NIS)	(in thousands NIS)	(in US $ thousands)
Cash and cash equivalents	17,506	14,622	4,278	20,767	36,091	9,280
Other receivables and lease deposit	550	3,760	1,672	2,195	3,443	886
Fixed assets	490	278	159	143	133	34
Total assets	18,546	18,660	6,109	23,105	39,667	10,200
Total liabilities	5,474	6,133	8,754	7,580	12,967	3,335
Total shareholders' equity	13,072	12,527	(2,645)	15,525	26,700	6,865

We report our financial statements in NIS. This Annual Report on Form 20-F contains conversions of NIS amounts into U.S. dollars at specific rates solely for the convenience of the reader. Unless otherwise noted, for the purposes of annual financial data, all conversions from NIS to U.S. dollars and from U.S. dollars to NIS were made at a rate of NIS 3.889 to $1.00 U.S. dollar, the daily representative rates in effect as of December 31, 2014. No representation is made that the NIS amounts referred to in this Annual Report on Form 20-F could have been or could be converted into U.S. dollars at any particular rate or at all.

The following table sets forth information regarding the exchange rates of U.S. dollars per NIS for the periods indicated. Average rates are calculated by using the daily representative rates as reported by the Bank of Israel on the last day of each month during the periods presented.

	NIS per U.S. $			
Year Ended December 31,	High	Low	Average	Period End
2014	3.994	3.402	3.578	3.889
2013	3.791	3.471	3.611	3.471
2012	4.084	3.700	3.858	3.733
2011	3.821	3.363	3.579	3.821
2010	3.894	3.549	3.732	3.549

The following table sets forth the high and low daily representative rates for the NIS as reported by the Bank of Israel for each of the prior six months.

	NIS per U.S. $			
Month Ended	High	Low	Average	Period End
March 2015 (through March 23, 2015)	4.053	3.984	4.017	4.018
February 2015	3.966	3.844	3.893	3.966
January 2015	3.998	3.899	3.946	3.924
December 2014	3.994	3.889	3.935	3.889
November 2014	3.889	3.782	3.829	3.889
October 2014	3.793	3.644	3.736	3.784
September 2014	3.695	3.578	3.627	3.695

On March 23, 2015, the closing representative rate was $1.00 to NIS 4.018, as reported by the Bank of Israel.

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors

You should carefully consider the risks we describe below, in addition to the other information set forth elsewhere in this Annual Report on Form 20-F, including our consolidated financial statements and the related notes beginning on page F-1, before deciding to invest in our ordinary shares and ADSs. These material risks could adversely impact our results of operations, possibly causing the trading price of our ordinary shares and ADSs to decline, and you could lose all or part of your investment.

Risks Related to Our Financial Position and Capital Requirements

We have incurred operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future.

We are a clinical stage biopharmaceutical company that develops orally bioavailable small molecule therapeutic products for the treatment of autoimmune-inflammatory, oncological and ophthalmic diseases. Since our incorporation in 1994, we have been focused on research and development activities with a view to developing our product candidates, CF101, CF102 and CF602. We have financed our operations primarily through the sale of equity securities (both in private placements and in public offerings on the Tel Aviv Stock Exchange, or TASE and NYSE MKT) and payments received under out- licensing agreements and have incurred losses in each year since our inception in 1994. We have historically incurred substantial net losses, including net losses of approximately NIS 24 million in 2014, NIS 31 million in 2013 and NIS 22 million in 2012. At December 31, 2014, we had an accumulated deficit of approximately NIS 304 million. We do not know whether or when we will become profitable. To date, we have not commercialized any products or generated any revenues from product sales and accordingly we do not have a revenue stream to support our cost structure. Our losses have resulted principally from costs incurred in development and discovery activities. We expect to continue to incur losses for the foreseeable future, and these losses will likely increase as we:

- initiate and manage pre-clinical development and clinical trials for our current and new product candidates;
- seek regulatory approvals for our product candidates;
- implement internal systems and infrastructures;
- seek to license additional technologies to develop;
- hire management and other personnel; and
- move towards commercialization.

If our product candidates fail in clinical trials or do not gain regulatory clearance or approval, or if our product candidates do not achieve market acceptance, we may never become profitable. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our inability to achieve and then maintain profitability would negatively affect our business, financial condition, results of operations and cash flows. Moreover, our prospects must be considered in light of the risks and uncertainties encountered by an early-stage company and in highly regulated and competitive markets, such as the biopharmaceutical market, where regulatory approval and market acceptance of our products are uncertain. There can be no assurance that our efforts will ultimately be successful or result in revenues or profits.

We will need to raise additional capital to meet our business requirements in the future, and such capital raising may be costly or difficult to obtain and will dilute current shareholders' ownership interests.

As of December 31, 2014, we had cash and cash equivalents of approximately $9.3 million. In March 2014, we closed a private placement for gross proceeds of approximately $5 million and in December 2014, we closed an $8 million at-the-market registered direct offering. We believe that our existing financial resources will be sufficient to meet our requirements for the next twelve months. We have expended and believe that we will continue to expend substantial resources for the foreseeable future developing our product candidates. These expenditures will include costs associated with research and development, manufacturing, conducting preclinical experiments and clinical trials and obtaining regulatory approvals, as well as commercializing any products approved for sale. In addition, we have agreed to provide certain financial support to our subsidiary, OphthaliX Inc., or OphthaliX, for the foreseeable future. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. In addition, other unanticipated costs may arise. As a result of these and other factors currently unknown to us, we will require additional funds, through public or private equity or debt financings or other sources, such as strategic partnerships and alliances and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements will depend on many factors, including the progress and results of our clinical trials, the duration and cost of discovery and preclinical development, and laboratory testing and clinical trials for our product candidates, the timing and outcome of regulatory review of our product candidates, the number and development requirements of other product candidates that we pursue, and the costs of activities, such as product marketing, sales, and distribution. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our anticipated clinical trials.

Our future capital requirements depend on many factors, including:

- the failure to obtain regulatory approval or achieve commercial success of our product candidates, including CF101, CF102 and CF602;
- the results of our preclinical studies and clinical trials for our earlier stage product candidates, and any decisions to initiate clinical trials if supported by the preclinical results;
- the costs, timing and outcome of regulatory review of our product candidates that progress to clinical trials;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our issued patents and defending intellectual property-related claims;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;
- the timing, receipt and amount of sales of, or royalties on, our future products, if any;

- the expenses needed to attract and retain skilled personnel;
- any product liability or other lawsuits related to our products;
- the extent to which we acquire or invest in businesses, products or technologies and other strategic relationships; and
- the costs of financing unanticipated working capital requirements and responding to competitive pressures.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

We may incur substantial costs in pursuing future capital financing, including investment banking fees, legal fees, accounting fees, securities law compliance fees, printing and distribution expenses and other costs. We may also be required to recognize non-cash expenses in connection with certain securities we issue, such as convertible notes and warrants, which may adversely impact our financial condition.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing shareholders will be diluted, and the terms may include liquidation or other preferences that adversely affect shareholder rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

If we fail to obtain necessary funds for our operations, we will be unable to maintain and improve our patented or licensed technology, and we will be unable to develop and commercialize our products and technologies.

Our present and future capital requirements depend on many factors, including:

- the level of research and development investment required to develop our product candidates, and maintain and improve our patented or licensed technology position;
- the costs of obtaining or manufacturing product candidates for research and development and testing;
- the results of preclinical and clinical testing, which can be unpredictable in product candidate development;
- changes in product candidate development plans needed to address any difficulties that may arise in manufacturing, preclinical activities or clinical studies;

- our ability and willingness to enter into new agreements with strategic partners and the terms of these agreements;
- our success rate in preclinical and clinical efforts associated with milestones and royalties;
- the costs of investigating patents that might block us from developing potential product candidates;
- the costs of recruiting and retaining qualified personnel;
- the time and costs involved in obtaining regulatory approvals;
- the number of product candidates we pursue;
- our revenues, if any;
- the costs of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- our need or decision to acquire or license complementary technologies or new platform or product candidate targets.

If we are unable to obtain the funds necessary for our operations, we will be unable to maintain and improve our patented technology, and we will be unable to develop and commercialize our products and technologies, which would materially and adversely affect our business, liquidity and results of operations.

Risks Related to our Business and Regulatory Matters

We have not yet commercialized any products or technologies, and we may never become profitable.

We have not yet commercialized any products or technologies, and we may never be able to do so. We do not know when or if we will complete any of our product development efforts, obtain regulatory approval for any product candidates incorporating our technologies or successfully commercialize any approved products. Even if we are successful in developing products that are approved for marketing, we will not be successful unless these products gain market acceptance for appropriate indications at favorable reimbursement rates. The degree of market acceptance of these products will depend on a number of factors, including:

- the timing of regulatory approvals in the countries, and for the uses, we seek;
- the competitive environment;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products;
- our ability to enter into strategic agreements with pharmaceutical and biotechnology companies with strong marketing and sales capabilities;
- the adequacy and success of distribution, sales and marketing efforts; and
- the pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, thirty-party payors or the medical community in general may be unwilling to accept, utilize or recommend, and in the case of third-party payors, cover any of our products or products incorporating our technologies. As a result, we are unable to predict the extent of future losses or the time required to achieve profitability, if at all. Even if we successfully develop one or more products that incorporate our technologies, we may not become profitable.

Our product candidates are at various stages of clinical and preclinical development and may never be commercialized.

Our product candidates are at various stages of clinical development and may never be commercialized. The progress and results of any future pre-clinical testing or future clinical trials are uncertain, and the failure of our product candidates to receive regulatory approvals will have a material adverse effect on our business, operating results and financial condition to the extent we are unable to commercialize any products. None of our product candidates has received regulatory approval for commercial sale. In addition, we face the risks of failure inherent in developing therapeutic products. Our product candidates are not expected to be commercially available for several years, if at all.

In addition, our product candidates must satisfy rigorous standards of safety and efficacy before they can be approved by the U.S. Food and Drug Administration, or the FDA, and foreign regulatory authorities for commercial use. The FDA and foreign regulatory authorities have full discretion over this approval process. We will need to conduct significant additional research, involving testing in animals and in humans, before we can file applications for product approval. Typically, in the pharmaceutical industry, there is a high rate of attrition for product candidates in pre-clinical testing and clinical trials. Also, satisfying regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. In addition, delays or rejections may be encountered based upon additional government regulation, including any changes in FDA policy, during the process of product development, clinical trials and regulatory reviews.

In order to receive FDA approval or approval from foreign regulatory authorities to market a product candidate or to distribute our products, we must demonstrate thorough pre-clinical testing and thorough human clinical trials that the product candidate is safe and effective for its intended uses (*e.g.*, treatment of a specific condition in a specific way subject to contradictions and other limitations). Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our new drug applications, or NDA, or grant approval for a narrowly intended use that is not commercially feasible. We might not obtain regulatory approval for our drug candidates in a timely manner, if at all. Failure to obtain FDA approval of any of our drug candidates in a timely manner or at all will severely undermine our business by reducing the number of salable products and, therefore, corresponding product revenues.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of preclinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. For example, in December 2013, Ophthalix, our subsidiary, announced top-line results of a Phase III study with CF 101 for dry-eye syndrome in which CF101 did not meet the primary efficacy endpoint of complete clearing of corneal staining, nor the secondary efficacy endpoints. In addition, two Phase IIb studies in rheumatoid arthritis, or RA, utilizing CF101 in combination with methotrexate, a generic drug commonly used for treating RA patients, or MTX, failed to reach their primary endpoints. Many companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies.Any delay in, or termination or suspension of, our clinical trials will delay the requisite filings with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. If the clinical trials do not support our product claims, the completion of development of such product candidates may be significantly delayed or abandoned, which will significantly impair our ability to generate product revenues and will materially adversely affect our results of operations.

This drug candidate development risk is heightened by any changes in the planned clinical trials compared to the completed clinical trials. As product candidates are developed from preclinical through early to late stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize processes and results. While these types of changes are common and are intended to optimize the product candidates for late stage clinical trials, approval and commercialization, such changes do carry the risk that they will not achieve these intended objectives.

Changes in our planned clinical trials or future clinical trials could cause our product candidates to perform differently, including causing toxicities, which could delay completion of our clinical trials, delay approval of our product candidates, and/or jeopardize our ability to commence product sales and generate revenues.

We might be unable to develop product candidates that will achieve commercial success in a timely and cost-effective manner, or ever.

Even if regulatory authorities approve our product candidates, they may not be commercially successful. Our product candidates may not be commercially successful because government agencies and other third-party payors may not cover the product or the coverage may be too limited to be commercially successful; physicians and others may not use or recommend our products, even following regulatory approval. A product approval, assuming one issues, may limit the uses for which the product may be distributed thereby adversely affecting the commercial viability of the product. Third parties may develop superior products or have proprietary rights that preclude us from marketing our products. We also expect that at least some of our product candidates will be expensive, if approved. Patient acceptance of and demand for any product candidates for which we obtain regulatory approval or license will depend largely on many factors, including but not limited to the extent, if any, of reimbursement of costs by government agencies and other third-party payors, pricing, the effectiveness of our marketing and distribution efforts, the safety and effectiveness of alternative products, and the prevalence and severity of side effects associated with our products. If physicians, government agencies and other third-party payors do not accept our products, we will not be able to generate significant revenue.

Our current pipeline is based on our platform technology utilizing the Gi protein associated A3 adenosine receptor, or A3AR, as a potent therapeutic target and currently includes three molecules, the CF101, CF102 and CF602 product candidates, of which CF 101 is the most advanced. Failure to develop these molecules will have a material adverse effect on us.

Our current pipeline is based on a platform technology where we target the A3AR with highly selective ligands, or small signal triggering molecules that bind to specific cell surface receptors, such as the A3AR, including CF101, CF102 and CF602, currently developed for the treatment of autoimmune-inflammatory, oncological and ophthalmic disorders. A3ARs are structures found in cell surfaces that record and transfer messages from small molecules or ligands, such as CF101, CF102 and CF602 to the rest of the cell. CF101 is the most advanced of our drug candidates. As such, we are currently dependent on only three molecules for our potential commercial success, and any safety or efficacy concerns related to such molecules would have a significant impact on our business. Failure to develop our drug candidates, in whole or in part, will have a material adverse effect on us.

Clinical trials are very expensive, time-consuming and difficult to design and implement, and, as a result, we may suffer delays or suspensions in future trials which would have a material adverse effect on our ability to generate revenues.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Regulatory authorities, such as the FDA, may preclude clinical trials from proceeding. Additionally, the clinical trial process is time-consuming, failure can occur at any stage of the trials, and we may encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- unforeseen safety issues;
- determination of dosing issues;

- lack of effectiveness or efficacy during clinical trials;
- failure of third party suppliers to perform final manufacturing steps for the drug substance;
- slower than expected rates of patient recruitment and enrollment;
- lack of healthy volunteers and patients to conduct trials;
- inability to monitor patients adequately during or after treatment;
- failure of third party contract research organizations to properly implement or monitor the clinical trial protocols;
- failure of institutional review boards to approve our clinical trial protocols;
- inability or unwillingness of medical investigators and institutional review boards to follow our clinical trial protocols; and
- lack of sufficient funding to finance the clinical trials.

We have experienced the risks involved with conducting clinical trials, including but not limited to, increased expense and delay and failure to meet end points of the trial. For example, in December 2013, Ophthalix, our subsidiary, announced top-line results of a Phase III study with CF 101 for dry-eye syndrome in which CF101 did not meet the primary efficacy endpoint of complete clearing of corneal staining, nor the secondary efficacy endpoints. In addition, two Phase IIb studies in RA, utilizing CF101 in combination with methotrexate, a generic drug commonly used for treating RA patients, or MTX, failed to reach their primary end points.

In addition, we or regulatory authorities may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the regulatory authorities find deficiencies in our regulatory submissions or the conduct of these trials. Any suspension of clinical trials will delay possible regulatory approval, if any, and adversely impact our ability to develop products and generate revenue.

If we acquire or license additional technology or product candidates, we may incur a number of costs, may have integration difficulties and may experience other risks that could harm our business and results of operations.

We may acquire and license additional product candidates and technologies. Any product candidate or technology we license from others or acquire will likely require additional development efforts prior to commercial sale, including extensive pre-clinical or clinical testing, or both, and approval by the FDA and applicable foreign regulatory authorities, if any. All product candidates are prone to risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate or product developed based on licensed technology will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any product candidate that we develop based on acquired or licensed technology that is granted regulatory approval will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace. Moreover, integrating any newly acquired product candidates could be expensive and time-consuming. If we cannot effectively manage these aspects of our business strategy, our business may not succeed.

The manufacture of our product candidates is a chemical synthesis process and if one of our materials suppliers encounters problems manufacturing our products, our business could suffer.

The FDA and foreign regulators require manufacturers to register manufacturing facilities. The FDA and foreign regulators also inspect these facilities to confirm compliance with requirements that the FDA or foreign regulators establish. We do not intend to engage in the manufacture of our products other than for pre-clinical and clinical studies, but we or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's or foreign regulators' requirements necessary to continue manufacturing our drug substance. Drug manufacturers are subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency, or DEA, and corresponding foreign regulators to ensure strict compliance with requirements and other governmental regulations and corresponding foreign standards. Any failure to comply with DEA requirements or FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to market and develop our product candidates.

We do not currently have sales, marketing or distribution capabilities or experience, and we are unable to effectively sell, market or distribute our product candidates now and we do not expect to be able to do so in the future. The failure to enter into agreements with third parties that are capable of performing these functions would have a material adverse effect on our business and results of operations.

We do not currently have and we do not expect to develop sales, marketing and distribution capabilities. If we are unable to enter into agreements with third parties to perform these functions, we will not be able to successfully market any of our platforms or product candidates. In order to successfully market any of our platform or product candidates, we must make arrangements with third parties to perform these services.

As we do not intend to develop a marketing and sales force with technical expertise and supporting distribution capabilities, we will be unable to market any of our product candidates directly. To promote any of our potential products through third parties, we will have to locate acceptable third parties for these functions and enter into agreements with them on acceptable terms, and we may not be able to do so. Any third-party arrangements we are able to enter into may result in lower revenues than we could achieve by directly marketing and selling our potential products. In addition, to the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, as well as the terms of our agreements with such third parties, which cannot be predicted in most cases at this time. As a result, we might not be able to market and sell our products in the United States or overseas, which would have a material adverse effect on us.

We will to some extent rely on third parties to implement our manufacturing and supply strategies. Failure of these third parties in any respect could have a material adverse effect on our business, results of operations and financial condition.

If our current and future manufacturing and supply strategies are unsuccessful, then we may be unable to conduct and complete any future pre-clinical or clinical trials or commercialize our product candidates in a timely manner, if at all. Completion of any potential future pre-clinical or clinical trials and commercialization of our product candidates will require access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We do not have the resources, facilities or experience to manufacture our product candidates for commercial purposes on our own and do not intend to develop or acquire facilities for the manufacture of product candidates for commercial purposes in the foreseeable future. We may rely on contract manufacturers to produce sufficient quantities of our product candidates necessary for any pre-clinical or clinical testing we undertake in the future. Such contract manufacturers may be the sole source of production and they may have limited experience at manufacturing, formulating, analyzing, filling and finishing our types of product candidates.

We also intend to rely on third parties to supply the requisite materials needed for the manufacturing of our active pharmaceutical ingredients, or API. There may be a limited supply of these requisite materials. We might not be able to enter into agreements that provide us assurance of availability of such components in the future from any supplier. Our potential suppliers may not be able to adequately supply us with the components necessary to successfully conduct our pre-clinical and clinical trials or to commercialize our product candidates. If we cannot acquire an acceptable supply of the requisite materials to produce our product candidates, we will not be able to complete pre-clinical and clinical trials and will not be able to market or commercialize our product candidates

We depend on key members of our management and key consultants and will need to add and retain additional leading experts. Failure to retain our management and consulting team and add additional leading experts could have a material adverse effect on our business, results of operations or financial condition.

We are highly dependent on our executive officers and other key management and technical personnel. Our failure to retain our Chief Executive Officer, Pnina Fishman, Ph.D., who has developed much of the technology we utilize today, or any other key management and technical personnel, could have a material adverse effect on our future operations. Our success is also dependent on our ability to attract, retain and motivate highly trained technical, and management personnel, among others, to continue the development and commercialization of our current and future products. We presently maintain a life insurance policy on our Chief Executive Officer, Pnina Fishman.

Our success also depends on our ability to attract, retain and motivate personnel required for the development, maintenance and expansion of our activities. There can be no assurance that we will be able to retain our existing personnel or attract additional qualified employees or consultants. The loss of key personnel or the inability to hire and retain additional qualified personnel in the future could have a material adverse effect on our business, financial condition and results of operation.

We face significant competition and continuous technological change, and developments by competitors may render our products or technologies obsolete or non-competitive. If we cannot successfully compete with new or existing products, our marketing and sales will suffer and we may not ever be profitable.

We will compete against fully integrated pharmaceutical and biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs than we do, and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking pre-clinical testing and human clinical trials;
- obtaining FDA, addressing various regulatory matters and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

If our competitors develop and commercialize products faster than we do, or develop and commercialize products that are superior to our product candidates, our commercial opportunities will be reduced or eliminated. The extent to which any of our product candidates achieve market acceptance will depend on competitive factors, many of which are beyond our control. Competition in the biotechnology and biopharmaceutical industry is intense and has been accentuated by the rapid pace of technology development. Our competitors include large integrated pharmaceutical companies, biotechnology companies that currently have drug and target discovery efforts, universities, and public and private research institutions. Almost all of these entities have substantially greater research and development capabilities and financial, scientific, manufacturing, marketing and sales resources than we do. These organizations also compete with us to:

- attract parties for acquisitions, joint ventures or other collaborations;
- license proprietary technology that is competitive with the technology we are developing;
- attract funding; and
- attract and hire scientific talent and other qualified personnel.

Our competitors may succeed in developing and commercializing products earlier and obtaining regulatory approvals from the FDA more rapidly than we do. Our competitors may also develop products or technologies that are superior to those we are developing, and render our product candidates or technologies obsolete or non-competitive. If we cannot successfully compete with new or existing products, our marketing and sales will suffer and we may not ever be profitable.

Our competitors currently include companies with marketed products and/or an advanced research and development pipeline. The major competitors in the arthritis and psoriasis therapeutic field include Abbott Laboratories, Johnson & Johnson, Amgen, Roche, Pfizer, Novartis, Astellas, Eli Lilly, Janssen and more. The competitive landscape in the ophthalmic therapeutics field includes Novartis/Alcon, Allergan, Pfizer, Roche/Genentech, Merck (which acquired Inspire Pharmaceuticals), Santen (which acquired Novagali), Bausch & Lomb (which acquired ISTA Pharmaceuticals and is currently being acquired by Valeant), GlaxoSmithKline, or GSK, Sanofi-Aventis (which acquired Fovea) and more. Competitors in the hepatocellular carcinoma, also known as primary liver cancer, or HCC field include companies such as Onyx, Bayer, Bristol-Myers Squibb, Abbott Laboratories, Eli Lilly, Arqule and more. Competitors in the hepatitis C virus, or HCV, field include companies such as Merck, Vertex, Roche, Bristol-Myers Squibb (which acquired Inhibitex), Gilead Sciences (which acquired Pharmasset), Achillion, Idenix, Valeant, Human Genome Sciences, Abbott Laboratories, AstraZeneca, BoehringerIngelheim, Novartis, Pfizer, Idenix, Johnson & Johnson, Presidio, Medivir, Celgene, Enanta, GSK and more. See "Item 4. Information on the Company—B. Business Overview—Competition."

Moreover, several companies have reported the commencement of research projects related to the A3AR. Such companies include CV Therapeutics Inc. (which was acquired by Gilead), King Pharmaceuticals R&D Inv. (which was acquired by Merck), Hoechst Marion Roussel Inc., Novo Nordisk A/S and Inotek Pharmaceuticals. However, we are not aware if such projects are ongoing or have been completed and, to the best of our knowledge, there is no approved drug currently on the market which is similar to our A3AR agonists, nor are we aware of any allosteric modulatorin the A3AR product pipeline similar to our allosteric modulator with respect to chemical profile and mechanism of action.

We may suffer losses from product liability claims if our product candidates cause harm to patients.

Any of our product candidates could cause adverse events. Although data from a pooled analysis of 730 patients (527 CF101, 203 placebo) indicates that CF101 is safe and well tolerated at doses up to 4.0 mg administered twice daily for up to 12 weeks, there were incidences (albeit less than or equal to 5%) of adverse events in five completed and fully analyzed trials in inflammatory disease. Such adverse events included nausea, diarrhea, constipation, common and viral syndromes (such as, tonsillitis, otitis and respiratory and urinary tract infections, myalgia, arthralgia, dizziness, headache, palpitations and pruritus. We observed an even lower incidence (less than or equal to 2%) of serious adverse events, including pancytopenia (although extensive evaluation suggests that such adverse event was associated with an inadvertent overdose of MTX), exacerbation of chronic obstructive lung disease and exacerbation of Parkinson's Disease. Notwithstanding the foregoing, the placebo group in such studies had a higher incidence of overall adverse events than any CF101 dose group and a higher incidence of drug-related adverse events than any CF101 dose group (with the exception of the 1.0 mg group). Safety data from 652 additional subjects treated with CF101 in 3 subsequent Phase II and Phase III trials are consistent with data from previous trials in showing a low incidence of adverse events associated with CF101 treatment, an absence of apparent dose-response of CF101-associated adverse events and incidences of most adverse events in the CF101 groups comparable to those in the placebo group. No new safety concerns have been identified and no novel or unexpected safety concerns have appeared over 24 weeks of treatment in more recent trials.In a trial of 19 patients with hepatocellular carcinoma dosed with CF102 for a median of 190 days, CF102 was generally well-tolerated. The most common CF102-related adverse events were fatigue (5 patients, 26.3%), asthenia and decreased appetite (4 patients each, 21.1%), and pyrexia and constipation (3 patients each, 15.8%).

There is also a risk that certain adverse events may not be observed in clinical trials, but may nonetheless occur in the future. If any of these adverse events occur, they may render our product candidates ineffective or harmful in some patients, and our sales would suffer, materially adversely affecting our business, financial condition and results of operations.

In addition, potential adverse events caused by our product candidates could lead to product liability lawsuits. If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit the marketing and commercialization of our product candidates. Our business exposes us to potential product liability risks, which are inherent in the testing, manufacturing, marketing and sale of pharmaceutical products. We may not be able to avoid product liability claims. Product liability insurance for the pharmaceutical and biotechnology industries is generally expensive, if available at all. If, at any time, we are unable to obtain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to clinically test, market or commercialize our product candidates. A successful product liability claim brought against us in excess of our insurance coverage, if any, may cause us to incur substantial liabilities, and, as a result, our business, liquidity and results of operations would be materially adversely affected.

Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with these requirements, we could lose these approvals, and the sales of any approved commercial products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the uses for which the product may be marketed or the conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, which could negatively impact us or our collaboration partners by reducing revenues or increasing expenses, and cause the approved product candidate not to be commercially viable. In addition, as clinical experience with a drug expands after approval, typically because it is used by a greater number and more diverse group of patients after approval than during clinical trials, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials or other studies. Any adverse effects observed after the approval and marketing of a product candidate could result in limitations on the use of or withdrawal of any approved products from the marketplace. Absence of long-term safety data may also limit the approved uses of our products, if any. If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including the following:

- Restrictions on the products, manufacturers or manufacturing process;
- Warning letters;
- Civil or criminal penalties, fines and injunctions;
- Product seizures or detentions;
- Import or export bans or restrictions;
- Voluntary or mandatory product recalls and related publicity requirements;
- Suspension or withdrawal of regulatory approvals;
- Total or partial suspension of production, and
- Refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

If we or our collaborators are slow or unable to adapt to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, marketing approval for our product candidates may be lost or cease to be achievable, resulting in decreased revenue from milestones, product sales or royalties, which would have a material adverse effect on our results of operations.

We deal with hazardous materials and must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do business.

Our activities and those of our third-party manufacturers on our behalf involve the controlled storage, use and disposal of hazardous materials, including corrosive, explosive and flammable chemicals and other hazardous compounds. We and our manufacturers are subject to U.S. federal, state, local, Israeli and other foreign laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In addition, if we develop a manufacturing capacity, we may incur substantial costs to comply with environmental regulations and would be subject to the risk of accidental contamination or injury from the use of hazardous materials in our manufacturing process.

In the event of an accident, government authorities may curtail our use of these materials and interrupt our business operations. In addition, we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Although our Israeli insurance program covers certain unforeseen sudden pollutions, we do not maintain a separate insurance policy for any of the foregoing types of risks. In addition, although the general liability section of our life sciences policy covers certain unforeseen, sudden environmental issues, pollution in the United States and Canada is excluded from the policy. In the event of environmental discharge or contamination or an accident, we may be held liable for any resulting damages, and any liability could exceed our resources. In addition, we may be subject to liability and may be required to comply with new or existing environmental laws regulating pharmaceuticals or other medical products in the environment.

We may not be able to successfully grow and expand our business. Failure to manage our growth effectively will have a material adverse effect on our business, results of operations and financial condition.

We may not be able to successfully grow and expand. Successful implementation of our business plan will require management of growth, which will result in an increase in the level of responsibility for management personnel. To manage growth effectively, we will be required to continue to implement and improve our operating and financial systems and controls to expand, train and manage our employee base. The management, systems and controls currently in place or to be implemented may not be adequate for such growth, and the steps taken to hire personnel and to improve such systems and controls might not be sufficient. If we are unable to manage our growth effectively, it will have a material adverse effect on our business, results of operations and financial condition.

We may encounter difficulties in managing our growth. These difficulties could increase our losses.

We may experience rapid and substantial growth in order to achieve our operating plans, which will place a strain on our human and capital resources. If we are unable to manage this growth effectively, our losses could materially increase. Our ability to manage our operations and growth effectively requires us to continue to expend funds to enhance our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. If we are unable to scale up and implement improvements to our control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, then we will not be able to make available the products required to successfully commercialize our technology. Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth or result in ineffective growth.

Our ability to effectively recruit and retain qualified officers and directors could also be adversely affected if we experience difficulty in obtaining adequate directors' and officers' liability insurance.

We may be unable to maintain sufficient insurance as a public company to cover liability claims made against our officers and directors. If we are unable to adequately insure our officers and directors, we may not be able to retain or recruit qualified officers and directors to manage our company.

Risks Related to Our Intellectual Property

We license from the National Institute of Health, or the NIH, and Leiden University intellectual property which protects certain small molecules which target the A3AR, in furtherance of our platform technology, and we could lose our rights to these licenses if a dispute with the NIH or Leiden University arises or if we fail to comply with the financial and other terms of the licenses.

We have licensed intellectual property from the NIH and Leiden University pursuant to license agreements, or the License Agreements, relating to molecules which target the A3AR. The License Agreements impose certain payment, reporting, confidentiality and other obligations on us. In the event that we were to breach any of the obligations and fail to cure, the NIH and Leiden University would have the right to terminate the respective License Agreement. In addition, the NIH and Leiden University each have the right to terminate the respective License Agreement upon our bankruptcy, insolvency, or receivership. Further, the NIH retains a paid-up, worldwide license to practice the licensed inventions for government purposes and may require us to grant sublicenses when necessary to fulfill health or safety needs and retains "march-in" rights, *i.e.*, the right to terminate the license, if, among other things, the invention is needed for a public use such as addressing a public health crisis or the licensee or sublicensee fails to take within a reasonable time to take effective steps to achieve practical application of the licensed invention. If any dispute arises with respect to our arrangements with the NIH and Leiden University, such dispute may disrupt our operations and would likely have a material adverse impact on us if resolved in a manner that is unfavorable to our Company. All of our current product candidates are partly based on the intellectual property licensed under the License Agreements, and if the License Agreements were terminated, it would have a material adverse effect on our business, prospects and results of operations.

The failure to obtain or maintain patents, licensing agreements, including our current licensing agreements, and other intellectual property could impact our ability to compete effectively.

To compete effectively, we need to develop and maintain a proprietary position with regard to our own technologies, intellectual property, licensing agreements, product candidates and business. Legal standards relating to the validity and scope of claims in the biotechnology and biopharmaceutical fields are still evolving. Therefore, the degree of future protection for our proprietary rights in our core technologies and any products that might be made using these technologies is also uncertain. The risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- while the patents we license have been issued, the pending patent applications we have filed may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference proceedings;
- we may be subject to opposition proceedings in foreign countries;
- any patents that are issued may not provide meaningful protection;
- we may not be able to develop additional proprietary technologies that are patentable;
- other companies may challenge patents licensed or issued to us or our customers;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed; and
- enforcement of patents is complex, uncertain and expensive.

We cannot be certain that patents will be issued as a result of any of our pending applications, and we cannot be certain that any of our issued patents, whether issued pursuant to our pending applications or licensed from the NIH and Leiden University, will give us adequate protection from competing products. For example, issued patents, including the patents licensed from the NIH and Leiden University, may be circumvented or challenged, declared invalid or unenforceable, or narrowed in scope. In addition, since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make our inventions or to file patent applications covering those inventions.

Moreover, the composition of matter patents pertaining to CF101 and CF102 that we licensed from the NIH expired on July 13, 2014 in Europe and will expire on June 30, 2015 in the United States. As of June 30, 2015, the License Agreement with the NIH will terminate. We do not expect that we will be able to submit an NDA seeking approval of CF101 or CF102 prior to the composition of matter patents' respective expiration dates. However, because CF101 and CF102 each may be a new chemical entity, or NCE, following approval of an NDA, we, if we are the first applicant to obtain NDA approval, may be entitled to five years of data and market exclusivity in the United States with respect to such NCEs. Analogous data and market exclusivity provisions, of varying duration, may be available in Europe and other foreign jurisdictions. We also have rights under our pharmaceutical use issued patents with respect to CF101 and CF102, which provide patent exclusivity within our field of activity until the mid- to late-2020s. While we believe that we may be able to protect our exclusivity in our field of activity through such use patent portfolio and such period of exclusivity, the lack of composition of matter patent protection may diminish our ability to maintain a proprietary position for our intended uses of CF101 and CF102. Moreover, we cannot be certain that we will be the first applicant to obtain an FDA approval for any indication of CF101 and we cannot be certain that we will be entitled to NCE exclusivity. Such diminution of our proprietary position could have a material adverse effect on our business, results of operation and financial condition.

It is also possible that others may obtain issued patents that could prevent us from commercializing our products or require us to obtain licenses requiring the payment of significant fees or royalties in order to enable us to conduct our business. As to those patents that we have licensed, our rights depend on maintaining our obligations to the licensor under the applicable license agreement, and we may be unable to do so.

In addition to patents and patent applications, we depend upon trade secrets and proprietary know-how to protect our proprietary technology. We require our employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to any other parties. We require our employees and consultants to disclose and assign to us their ideas, developments, discoveries and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure.

Costly litigation may be necessary to protect our intellectual property rights and we may be subject to claims alleging the violation of the intellectual property rights of others.

We may face significant expense and liability as a result of litigation or other proceedings relating to patents and other intellectual property rights of others. In the event that another party has also filed a patent application or been issued a patent relating to an invention or technology claimed by us in pending applications, we may be required to participate in an interference proceeding declared by the U.S. Patent and Trademark Office to determine priority of invention, which could result in substantial uncertainties and costs for us, even if the eventual outcome were favorable to us. We, or our licensors, also could be required to participate in interference proceedings involving issued patents and pending applications of another entity. An adverse outcome in an interference proceeding could require us to cease using the technology or to license rights from prevailing third parties.

The cost to us of any patent litigation or other proceeding relating to our licensed patents or patent applications, even if resolved in our favor, could be substantial. Our ability to enforce our patent protection could be limited by our financial resources, and may be subject to lengthy delays. If we are unable to effectively enforce our proprietary rights, or if we are found to infringe the rights of others, we may be in breach of our License Agreement.

A third party may claim that we are using inventions claimed by their patents and may go to court to stop us from engaging in our normal operations and activities, such as research, development and the sale of any future products. Such lawsuits are expensive and would consume time and other resources. There is a risk that the court will decide that we are infringing the third party's patents and will order us to stop the activities claimed by the patents, redesign our products or processes to avoid infringement or obtain licenses (which may not be available on commercially reasonable terms). In addition, there is a risk that a court will order us to pay the other party damages for having infringed their patents.

Moreover, there is no guarantee that any prevailing patent owner would offer us a license so that we could continue to engage in activities claimed by the patent, or that such a license, if made available to us, could be acquired on commercially acceptable terms. In addition, third parties may, in the future, assert other intellectual property infringement claims against us with respect to our product candidates, technologies or other matters.

We rely on confidentiality agreements that could be breached and may be difficult to enforce, which could result in third parties using our intellectual property to compete against us.

Although we believe that we take reasonable steps to protect our intellectual property, including the use of agreements relating to the non-disclosure of confidential information to third parties, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them, the agreements can be difficult and costly to enforce. Although we seek to obtain these types of agreements from our contractors, consultants, advisors and research collaborators, to the extent that employees and consultants utilize or independently develop intellectual property in connection with any of our projects, disputes may arise as to the intellectual property rights associated with our products. If a dispute arises, a court may determine that the right belongs to a third party. In addition, enforcement of our rights can be costly and unpredictable. We also rely on trade secrets and proprietary know-how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors or others. Despite the protective measures we employ, we still face the risk that:

- these agreements may be breached;
- these agreements may not provide adequate remedies for the applicable type of breach;
- our trade secrets or proprietary know-how will otherwise become known; or
- our competitors will independently develop similar technology or proprietary information.

International patent protection is particularly uncertain, and if we are involved in opposition proceedings in foreign countries, we may have to expend substantial sums and management resources.

Patent law outside the United States is in some cases different than in the United States and is currently undergoing review and revision in many countries. Further, the laws of some foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States. For example, certain countries do not grant patent claims that are directed to the treatment of humans. We may participate in opposition proceedings to determine the validity of our foreign patents or our competitors' foreign patents, which could result in substantial costs and diversion of our efforts.

Although most jurisdictions in which we have applied for, intend to apply for, or have been issued patents have patent protection laws similar to those of the United States, some of them do not. For example, we expect to do business in Brazil and India in the future. However, the Brazilian drug regulatory agency, ENVISA, has the authority to nullify patents on the basis of its perceived public interest and the Indian patent law does not allow patent protection for new uses of pharmaceuticals (many of our current patent applications are of such nature). Additionally, due to uncertainty in patent protection law, we have not filed applications in many countries where significant markets exist, including Indonesia, Pakistan, Russia, African countries and Taiwan.

We may be unable to protect the intellectual property rights of the third parties from whom we license certain of our intellectual property or with whom we have entered into other strategic relationships.

Certain of our intellectual property rights are currently licensed from the NIH and Leiden University, and, in the future, we intend to continue to license intellectual property from the NIH and Leiden University and/or other universities and/or strategic partners. Such third parties may determine not to protect the intellectual property rights that we license from them and we may be unable defend such intellectual property rights on our own or we may have to undertake costly litigation to defend the intellectual property rights of such third parties. There can be no assurances that we will continue to have proprietary rights to any of the intellectual property that we license from such third parties or otherwise have the right to use through similar strategic relationships. Any loss or limitations on use with respect to our right to use such intellectual property licensed from third parties or otherwise obtained from third parties with whom we have entered into strategic relationships could have a material adverse effect on our business, results of operations and financial condition.

Under current U.S. and Israeli law, we may not be able to enforce employees' covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees.

We have entered into non-competition agreements with our key employees, in most cases within the framework of their employment agreements. These agreements prohibit our key employees, if they cease working for us, from competing directly with us or working for our competitors for a limited period. Under applicable U.S. and Israeli law, we may be unable to enforce these agreements. If we cannot enforce our non-competition agreements with our employees, then we may be unable to prevent our competitors from benefiting from the expertise of our former employees, which could materially adversely affect our business, results of operations and ability to capitalize on our proprietary information.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- We or our licensors or any future strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- We or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- It is possible that our pending patent applications will not lead to issued patents;
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- We may not develop additional proprietary technologies that are patentable; and
- The patents of others may have an adverse effect on our business.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. In addition, the Israeli Supreme Court ruled in 2012 that an employee who receives a patent or contributes to an invention during his employment may be allowed to seek compensation for it from their employer, even if the employee's contract of employment specifically states otherwise and the employee has transferred all intellectual property rights to the employer. The Israeli Supreme Court ruled that the fact that a contract revokes the employee's right for royalties and compensation, does not rule out the right of the employee to claim their right for royalties. As a result, it is unclear if, and to what extent, our employees may be able to claim compensation with respect to our future revenue. As a result, we may receive less revenue from future products if such claims are successful which in turn could impact our future profitability.

Risks Related to Our Industry

We are subject to government regulations and we may experience delays in obtaining required regulatory approvals in the United States to market our proposed product candidates.

Various aspects of our operations are subject to federal, state or local laws, rules and regulations, any of which may change from time to time. Costs arising out of any regulatory developments could be time-consuming and expensive and could divert management resources and attention and, consequently, could adversely affect our business operations and financial performance.

Delays in regulatory approval, limitations in regulatory approval and withdrawals of regulatory approval may have a material adverse effect on us. If we experience significant delays in testing or receiving approvals or sign-offs to conduct clinical trials, our product development costs, or our ability to license product candidates, will increase. If the FDA grants regulatory approval to market a product, this approval will be limited to those disease states and conditions for which the product has demonstrated, through clinical trials, to be safe and effective. Any product approvals that we receive in the future could also include significant restrictions on the use or marketing of our products. Product approvals, if granted, can be withdrawn for failure to comply with regulatory requirements or upon the occurrence of adverse events following commercial introduction of the products. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our product candidates or us. If approval is withdrawn for a product, or if a product were seized or recalled, we would be unable to sell or license that product and our revenues would suffer. In addition, outside the United States, our ability to market any of our potential products is contingent upon receiving market application authorizations from the appropriate regulatory authorities and these foreign regulatory approval processes include all of the risks associated with the FDA approval process described above.

We expect the healthcare industry to face increased limitations on reimbursement as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.

In both the United States and other countries, sales of our products will depend in part upon the availability of reimbursement from third-party payors, which include governmental authorities, managed care organizations and other private health insurers. Third-party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in Congress and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In 2010, the United States Congress enacted the Patient Protection and Affordable Care Act of 2010 or, Affordable Care Act. The Affordable Care Act seeks to reduce the federal deficit and the rate of growth in health care spending through, among other things, stronger prevention and wellness measures, increased access to primary care, changes in health care delivery systems and the creation of health insurance exchanges. Enrollment in the health insurance exchanges began in October 2013. The Affordable Care Act requires the pharmaceutical industry to share in the costs of reform, by, among other things, increasing Medicaid rebates and expanding Medicaid rebates to cover Medicaid managed care programs. Other components of healthcare reform include funding of pharmaceutical costs for Medicare patients in excess of the prescription drug coverage limit and below the catastrophic coverage threshold. Under the Affordable Care Act, pharmaceutical companies are now obligated to fund 50% of the patient obligation for branded prescription pharmaceuticals in this gap, or "donut hole." Additionally, commencing in 2011, an excise tax was levied against certain branded pharmaceutical products. The tax is specified by statute to be approximately $3 billion in 2012 through 2016, $3.5 billion in 2017, $4.2 billion in 2018, and $2.8 billion each year thereafter. The tax is to be apportioned to qualifying pharmaceutical companies based on an allocation of their governmental programs as a portion of total pharmaceutical government programs.

Although we cannot predict the full effect on our business of the implementation of existing legislation, including the Affordable Care Act or the enactment of additional legislation, we believe that legislation or regulations that reduce reimbursement for or restrict coverage of our products could adversely affect how much or under what circumstances healthcare providers will prescribe or administer our products. This could materially and adversely affect our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales.

We are subject to federal anti-kickback laws and regulations. Our failure to comply with these laws and regulations could have adverse consequences to us.

There are extensive U.S. federal and state laws and regulations prohibiting fraud and abuse in the healthcare industry that can result in significant criminal and civil penalties. These federal laws include: the anti-kickback statute, which prohibits certain business practices and relationships, including the payment or receipt of remuneration for the referral of patients whose care will be paid by Medicare or other federal healthcare programs; the physician self-referral prohibition, commonly referred to as the Stark Law; the anti-inducement law, which prohibits providers from offering anything to a Medicare or Medicaid beneficiary to induce that beneficiary to use items or services covered by either program; the False Claims Act, which prohibits any person from knowingly presenting or causing to be presented false or fraudulent claims for payment by the federal government, including the Medicare and Medicaid programs; and the Civil Monetary Penalties Law, which authorizes the U.S. Department of Health and Human Services to impose civil penalties administratively for fraudulent or abusive acts.

Sanctions for violating these federal laws include criminal and civil penalties that range from punitive sanctions, damage assessments, money penalties, imprisonment, denial of Medicare and Medicaid payments, or exclusion from the Medicare and Medicaid programs, or both, and debarment. As federal and state budget pressures continue, federal and state administrative agencies may also continue to escalate investigation and enforcement efforts to root out waste and to control fraud and abuse in governmental healthcare programs. Private enforcement of healthcare fraud has also increased, due in large part to amendments to the civil False Claims Act in 1986 that were designed to encourage private persons to sue on behalf of the government. A violation of any of these federal and state fraud and abuse laws and regulations could have a material adverse effect on our liquidity and financial condition. An investigation into the use by physicians of any of our products once commercialized may dissuade physicians from either purchasing or using them, and could have a material adverse effect on our ability to commercialize those products.

Risks Related to our Ordinary Shares and ADSs

We may be a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in 2014 or in any subsequent year. There may be negative tax consequences for U.S. taxpayers that are holders of our ordinary shares or the ADSs.

We will be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of our gross income is "passive income" or (ii) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in a public offering. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account. We believe we may be a PFIC during 2014and although we have not determined whether we will be a PFIC in 2015, or in any subsequent year, our operating results for any such years may cause us to be a PFIC. If we are a PFIC in 2014, or any subsequent year, and a U.S. shareholder does not make an election to treat us as a "qualified electing fund," or QEF, or make a "mark-to-market" election, then "excess distributions" to a U.S. shareholder, and any gain realized on the sale or other disposition of our ordinary shares or ADSs will be subject to special rules. Under these rules: (i) the excess distribution or gain would be allocated ratably over the U.S. shareholder's holding period for the ordinary shares (or ADSs, as the case may be); (ii) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (iii) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. In addition, if the U.S. Internal Revenue Service determines that we are a PFIC for a year with respect to which we have determined that we were not a PFIC, it may be too late for a U.S. shareholder to make a timely QEF or mark-to-market election. U.S. shareholders who hold our ordinary shares or ADSs during a period when we are a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to exceptions for U.S. shareholders who made a timely QEF or mark-to-market election. A U.S. shareholder can make a QEF election by completing the relevant portions of and filing IRS Form 8621 in accordance with the instructions thereto. Upon request, we will annually furnish U.S. shareholders with information needed in order to complete IRS Form 8621 (which form would be required to be filed with the IRS on an annual basis by the U.S. shareholder) and to make and maintain a valid QEF election for any year in which we or any of our subsidiaries that we control is a PFIC.

The market price of our ordinary shares is, and the market price of the ADSs will be, subject to fluctuation, which could result in substantial losses by our investors.

The stock market in general and the market price of our ordinary shares on the TASE, in particular, is subject to fluctuation, and changes in our share price may be unrelated to our operating performance. The market price of our ordinary shares on the TASE has fluctuated in the past, and we expect it will continue to do so. It is likely that the market price of the ADSs will likewise be subject to wide fluctuations. The market price of our ordinary shares and ADSs are and will be subject to a number of factors, including:

- announcements of technological innovations or new products by us or others;
- announcements by us of significant strategic partnerships, out-licensing, in-licensing, joint ventures, acquisitions or capital commitments;
- expiration or terminations of licenses, research contracts or other collaboration agreements;
- public concern as to the safety of drugs we, our licensees or others develop;
- general market conditions;
- the volatility of market prices for shares of biotechnology companies generally;
- success of research and development projects;
- success in clinical and preclinical studies;
- departure of key personnel;

- developments concerning intellectual property rights or regulatory approvals;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our ordinary shares or ADSs are covered by analysts;
- changes in government regulations or patent decisions;
- developments by our licensees; and
- general market conditions and other factors, including factors unrelated to our operating performance.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our ordinary shares and the ADSs and result in substantial losses by our investors.

Additionally, market prices for securities of biotechnology and pharmaceutical companies historically have been very volatile. The market for these securities has from time to time experienced significant price and volume fluctuations for reasons unrelated to the operating performance of any one company. In the past, following periods of market volatility, shareholders have often instituted securities class action litigation. If we were involved in securities litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful. Future sales of our ordinary shares or ADSs could reduce the market price of our ordinary shares and ADSs.

Substantial sales of our ordinary shares or the ADSs either on the TASE or on the NYSE MKT, as applicable, may cause the market price of our ordinary shares or the ADSs to decline.

Sales by us or our security-holders of substantial amounts of our ordinary shares or the ADSs, or the perception that these sales may occur in the future, could cause a reduction in the market price of our ordinary shares or the ADSs. The issuance of any additional ordinary shares or ADSs, or any securities that are exercisable for or convertible into our ordinary shares or the ADSs, may have an adverse effect on the market price of our ordinary shares or the ADSs, as applicable, and will have a dilutive effect on our shareholders.

ADS holders are not shareholders and do not have shareholder rights.

The Bank of New York Mellon, as Depositary, delivers the ADSs. Each ADS represents two of our ordinary shares. ADS holders will not be treated as shareholders and do not have the rights of shareholders. The depositary will be the holder of the shares underlying the ADSs. Holders of ADSs will have ADS holder rights. A deposit agreement among us, the depositary, ADS holders and the beneficial owners of ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs. Our shareholders have shareholder rights. Israeli law and our Articles of Association govern shareholder rights. ADS holders do not have the same voting rights as our shareholders. Shareholders are entitled to our notices of general meetings and to attend and vote at our general meetings of shareholders. At a general meeting, every shareholder present (in person or by proxy, attorney or representative) and entitled to vote has one vote. This is subject to any other rights or restrictions which may be attached to any shares. ADS holders may instruct the depositary how to vote the number of deposited shares their ADSs represent. *Otherwise you won't be able to exercise your right to vote unless you withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares.* The depositary will notify ADS holders of shareholders' meetings and arrange to deliver our voting materials to them if we ask it to. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the depositary how to vote. For instructions to be valid, they must reach the depositary by a date set by the depositary. The depositary will try, as far as practical, subject to the laws of Israel and our articles of association or similar documents, to vote or to have its agents vote the shares or other deposited securities as instructed by ADS holders. The depositary will only vote or attempt to vote as instructed. We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your hares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the matter of carrying out voting instructions. *This means that you may not be able to exercise your right to vote and there may be nothing you can do if your shares are not voted as requested.*

ADS holders do not have the same rights to receive dividends or other distributions as our shareholders. Subject to any special rights or restrictions attached to a share, the directors may determine that a dividend will be payable on a share and fix the amount, the time for payment and the method for payment (although we have never declared or paid any cash dividends on our ordinary shares and we do not anticipate paying any cash dividends in the foreseeable future). Dividends and other distributions payable to our shareholders with respect to our ordinary shares generally will be payable directly to them. Any dividends or distributions payable with respect to ordinary shares deposited in the ADS facility will be paid to the depositary, which has agreed to pay to ADS holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after deducting its fees and expenses. ADS holders will receive these distributions in proportion to the number of ordinary shares their ADSs represent. In addition, there may be certain circumstances in which the depositary may not pay ADS holders amounts distributed by us as a dividend or distribution.

Our ordinary shares and the ADSs are traded on different markets and this may result in price variations.

Our ordinary shares have traded on the TASE since October 2005 and the ADSs have been listed on the NYSE MKT since November 2013. Trading on these markets will take place in different currencies (U.S. dollars on the NYSE MKT and NIS on the TASE), and at different times (resulting from different time zones, different trading days and different public holidays in the United States and Israel). The trading prices of our securities on these two markets may differ due to these and other factors. Any decrease in the price of our securities on one of these markets could cause a decrease in the trading price of our securities on the other market.

The ADSs have a limited prior trading history in the United States, and an active market may not develop, which may limit the ability of our investors to sell the ADSs in the United States.

There is a limited public market for the ADSs in the United States. Although we recently listed the ADSs on the NYSE MKT, the ADSs are thinly traded and an active trading market for the ADSs may never develop or may not be sustained if one develops. If an active market for the ADSs does not develop or is not sustained, it may be difficult to sell your ADSs.

We have incurred significant additional increased costs as a result of the listing of ADSs for trading on the NYSE MKT, and our management is required to devote substantial time to new compliance initiatives as well as to compliance with ongoing U.S. and Israeli reporting requirements.

As a public company in the United States, we incur additional significant accounting, legal and other expenses that we did not incur before becoming a reporting company in the United States. We also incur costs associated with corporate governance requirements of the SEC and the NYSE MKT Company Guide, as well as requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act as a result of ADSs being listed on the NYSE MKT. These rules and regulations have increased our legal and financial compliance costs, introduced new costs such as investor relations, stock exchange listing fees and shareholder reporting, and made some activities more time consuming and costly. The implementation and testing of such processes and systems may require us to hire outside consultants and incur other significant costs. Any future changes in the laws and regulations affecting public companies in the United States and Israel, including Section 404 and other provisions of the Sarbanes-Oxley Act, the rules and regulations adopted by the SEC and the NYSE MKT Company Guide, as well as applicable Israeli reporting requirements, for so long as they apply to us, may result in increased costs to us as we respond to such changes. These laws, rules and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our board committees or as executive officers.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of applicable SEC and NYSE MKT requirements, which may result in less protection than is accorded to investors under rules applicable to domestic issuers.

As a foreign private issuer, we will be permitted to follow certain home country corporate governance practices instead of those otherwise required under the NYSE MKT Company Guide for domestic issuers. For instance, we may follow home country practice in Israel with regard to, among other things, composition and function of the audit committee and other committees of our Board of Directors and certain general corporate governance matters. In addition, in certain instances we will follow our home country law, instead of the NYSE MKT Company Guide, which requires that we obtain shareholder approval for certain dilutive events, such as an issuance that will result in a change of control of the company, certain transactions other than a public offering involving issuances of a 20% or more interest in the company and certain acquisitions of the stock or assets of another company. We comply with the director independence requirements of the NYSE MKT Company Guide, including the requirement that a majority of the Board of Directors be independent, and make the required affirmative determination thereunder upon filing the listing application with the NYSE MKT. Following our home country governance practices as opposed to the requirements that would otherwise apply to a United States company listed on the NYSE MKT may provide less protection than is accorded to investors under the NYSE MKT Company Guide applicable to domestic issuers.

In addition, as a foreign private issuer, we will be exempt from the rules and regulations under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act, related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders will be exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic companies whose securities are registered under the Exchange Act.

Because we became a reporting company under the Exchange Act by means of filing a Form 20-F, we may have difficulty attract the attention of research analysts at major brokerage firms.

Because we did not become a reporting company by conducting an underwritten initial public offering in the U.S., we may have difficulty attracting the attention of security analysts at major brokerage firms in order for them to provide coverage of our company. The failure to receive research coverage or support in the market for our shares will have an adverse effect on our ability to develop a liquid market for the ADSs.

If we are unable to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act as they apply to a foreign private issuer that is listing on a U.S. exchange for the first time, or our internal control over financial reporting is not effective, the reliability of our financial statements may be questioned and our share price and the ADS price may suffer.

We have become subject to the requirements of the Sarbanes-Oxley Act since the ADSs are listed on the NYSE MKT. Section 404 of the Sarbanes-Oxley Act requires companies subject to the reporting requirements of the U.S. securities laws to do a comprehensive evaluation of its and its subsidiaries' internal control over financial reporting. To comply with this statute, we must document and test our internal control procedures and our management and issue a report concerning our internal control over financial reporting. In addition, under the JOBS Act, emerging growth companies, like ourselves, are exempt from certain reporting requirements, including the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. Under this exemption, our auditor will not be required to attest to and report on our management's assessment of our internal control over financial reporting during a five-year transition period. We will need to prepare for compliance with Section 404 by strengthening, assessing and testing our system of internal controls to provide the basis for our report. However, the continuous process of strengthening our internal controls and complying with Section 404 is complicated and time-consuming. Furthermore, as our business continues to grow both domestically and internationally, our internal controls will become more complex and will require significantly more resources and attention to ensure our internal controls remain effective overall. During the course of the testing, our management may identify material weaknesses or significant deficiencies, which may not be remedied in a timely manner to meet the deadline imposed by the Sarbanes-Oxley Act. If our management cannot favorably assess the effectiveness of our internal control over financial reporting, or our independent registered public accounting firm identifies material weaknesses in our internal controls, investor confidence in our financial results may weaken, and the market price of our securities may suffer.

As an "emerging growth company" under the JOBS Act, we are permitted to, and intend to, rely on exemptions from certain disclosure requirements.

As an "emerging growth company" under the JOBS Act, we are permitted to, and intend to, rely on exemptions from certain disclosure requirements. We are an emerging growth company until the earliest of: (i) the last day of the fiscal year during which we had total annual gross revenues of $1 billion or more, (ii) the last day of the fiscal year following the fifth anniversary of the date of the first sale of our common stock pursuant to an effective registration statement, (iii) the date on which we have, during the previous three-year period, issued more than $1 billion in non-convertible debt or (iv) the date on which we are deemed a "large accelerated issuer" as defined in Regulation S-K of the Securities Act. For so long as we remain an emerging growth company, we will not be required to:

- have an auditor report on our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act;
- comply with any requirement that may be adopted by the Public Company Accounting Oversight Board, or the PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis);
- submit certain executive compensation matters to shareholders advisory votes pursuant to the "say on frequency" and "say on pay" provisions (requiring a non-binding shareholder vote to approve compensation of certain executive officers) and the "say on golden parachute" provisions (requiring a non-binding shareholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010; and
- include detailed compensation discussion and analysis in our filings under the Exchange Act, and instead may provide a reduced level of disclosure concerning executive compensation.

Although we intend to rely on the exemptions provided in the JOBS Act, the exact implications of the JOBS Act for us are still subject to interpretations and guidance by the SEC and other regulatory agencies. In addition, as our business grows, we may no longer satisfy the conditions of an emerging growth company. We are currently evaluating and monitoring developments with respect to these new rules and we cannot assure you that we will be able to take advantage of all of the benefits from the JOBS Act.

Risks Related to our Operations in Israel

We conduct our operations in Israel and therefore our results may be adversely affected by political, economic and military instability in Israel and its region.

Our headquarters, all of our operations and some of our suppliers and third party contractors are located in central Israel and our key employees, officers and most of our directors are residents of Israel. Accordingly, political, economic and military conditions in Israel and the surrounding region may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. Any hostilities involving Israel or the interruption or curtailment of trade within Israel or between Israel and its trading partners could adversely affect our operations and results of operations and could make it more difficult for us to raise capital. During the winter of 2008, winter of 2012 and the summer of 2014, Israel was engaged in an armed conflict with Hamas, a militia group and political party operating in the Gaza Strip, and during the summer of 2006, Israel was engaged in an armed conflict with Hezbollah, a Lebanese Islamist Shiite militia group and political party. These conflicts involved missile strikes against civilian targets in various parts of Israel, and negatively affected business conditions in Israel. Recent political uprisings and social unrest in various countries in the Middle East and North Africa are affecting the political stability of those countries. This instability may lead to deterioration of the political relationships that exist between Israel and these countries, and have raised concerns regarding security in the region and the potential for armed conflict. Any armed conflicts, terrorist activities or political instability in the region could adversely affect business conditions and could harm our results of operations. For example, any major escalation in hostilities in the region could result in a portion of our employees and service providers being called up to perform military duty for an extended period of time. Parties with whom we do business have sometimes declined to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements.

Our commercial insurance does not cover losses that may occur as a result of events associated with the security situation in the Middle East. Although the Israeli government currently covers the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained. Any losses or damages incurred by us could have a material adverse effect on our business. Any armed conflicts or political instability in the region would likely negatively affect business conditions and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjected to an economic boycott. Several countries still restrict business with the State of Israel and with Israeli companies. These restrictive laws and policies may have an adverse impact on our operating results, financial condition or the expansion of our business.

Our operations may be disrupted as a result of the obligation of Israeli citizens to perform military service.

Many Israeli citizens, including Motti Farbstein, our Chief Operating and Financial Officer, are obligated to perform one month, and in some cases more, of annual military reserve duty until they reach the age of 45 (or older, for reservists with certain occupations) and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be military reserve duty call-ups in the future. Our operations could be disrupted by such call-ups, which may include the call-up of Motti Farbstein. Such disruption could materially adversely affect our business, financial condition and results of operations.

Because a certain portion of our expenses is incurred in currencies other than the NIS, our results of operations may be harmed by currency fluctuations and inflation.

Our reporting and functional currency is the NIS, and we pay a substantial portion of our expenses in NIS. Part of our expenses are payable in U.S. dollars or in Euros as well asthe revenues from our licensing arrangements that are payable in U.S. dollars and Canadian dollars, we expect our revenues from future licensing arrangements to be denominated in U.S. dollars or in Euros. As a result, we are exposed to the currency fluctuation risks relating to the recording of our revenues in NIS. For example, if the NIS strengthens against either the U.S. dollar or the Euro, our reported revenues in NIS may be lower than anticipated. The Israeli rate of inflation has not offset or compounded the effects caused by fluctuations between the NIS and the U.S. dollar or the Euro. To date, we have not engaged in hedging transactions. Although the Israeli rate of inflation has not had a material adverse effect on our financial condition during 2012, 2013, or 2014 to date, we may, in the future, decide to enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of the currencies mentioned above in relation to the NIS. These measures, however, may not adequately protect us from material adverse effects.

Provisions of Israeli law may delay, prevent or otherwise impede a merger with, or an acquisition of, our Company, which could prevent a change of control, even when the terms of such a transaction are favorable to us and our shareholders.

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to these types of transactions. For example, a merger may not be consummated unless at least 50 days have passed from the date that a merger proposal was filed by each merging company with the Israel Registrar of Companies and at least 30 days from the date that the shareholders of both merging companies approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, a full tender offer can only be completed if the acquirer receives at least 95% of the issued share capital; provided that, pursuant to an amendment to the Israeli Companies Law, effective as of May 15, 2011, a majority of the offerees that do not have a personal interest in such tender offer shall have approved the tender offer; except that, if the total votes to reject the tender offer represent less than 2% of our issued and outstanding share capital, in the aggregate, approval by a majority of the offerees that do not have a personal interest in such tender offer is not required to complete the tender offer), and the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition the court to alter the consideration for the acquisition (unless the acquirer stipulated in the tender offer that a shareholder that accepts the offer may not seek appraisal rights).

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of numerous conditions, including a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are restricted. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no actual disposition of the shares has occurred.

These and other similar provisions could delay, prevent or impede an acquisition of us or our merger with another company, even if such an acquisition or merger would be beneficial to us or to our shareholders. See "Item 10. Additional Information — Memorandum and Articles of Association."

It may be difficult to enforce a U.S. judgment against us and our officers and directors named in this Annual Report on Form 20-F in Israel or the United States, or to serve process on our officers and directors.

We are incorporated in Israel. All of our executive officers and directors listed in this Annual Report on Form 20-F reside outside of the United States, and all of our assets and most of the assets of our executive officers and directors are located outside of the United States. Therefore, a judgment obtained against us or most of our executive officers and all of our directors in the United States, including one based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the United States and may not be enforced by an Israeli court. It also may be difficult for you to effect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel.

Your rights and responsibilities as a shareholder will be governed by Israeli law which may differ in some respects from the rights and responsibilities of shareholders of U.S. companies.

We are incorporated under Israeli law. The rights and responsibilities of the holders of our ordinary shares and ADSs are governed by our Articles of Association and Israeli law. These rights and responsibilities differ in some respects from the rights and responsibilities of shareholders in typical U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith toward the company and other shareholders and to refrain from abusing its power in the company, including, among other things, in voting at the general meeting of shareholders on matters such as amendments to a company's articles of association, increases in a company's authorized share capital, mergers and acquisitions and interested party transactions requiring shareholder approval. In addition, a shareholder who knows that it possesses the power to determine the outcome of a shareholder vote or to appoint or prevent the appointment of a director or executive officer in the company has a duty of fairness toward the company. There is limited case law available to assist us in understanding the implications of these provisions that govern shareholders' actions. These provisions may be interpreted to impose additional obligations and liabilities on holders of our ordinary shares and ADSs that are not typically imposed on shareholders of U.S. corporations.

ITEM 4. Information on the Company

A. History and Development of the Company

Our legal name is Can-FiteBio Pharma Ltd. and our commercial name is "Can-Fite." We are a company limited by shares organized under the laws of the State of Israel. Our principal executive offices are located at 10 Bareket Street, Kiryat Matalon, Petah-Tikva 4951778 Israel. Our telephone number is +972 (3) 924-1114.

We were founded on September 11, 1994 by Pnina Fishman, Ph.D., our Chief Executive Officer and a director, and Ilan Cohn, Ph.D., our Vice-Chairman of the Board of Directors, under the name Can-Fite Technologies Ltd. On January 7, 2001, we changed our name to Can-FiteBio Pharma Ltd. We completed our initial public offering in Israel in October 2005 and our ordinary shares are traded on the TASE under the symbol "CFBI". On October 2, 2012, our ADSs began trading over the counter, or OTC, in the United States under the symbol "CANFY" and on November 19, 2013,our ADSs began trading on the NYSE MKT under the symbol "CANF."

In November 2011, through a series of transactions, we spun-off our activity in the ophthalmic field to OphthaliX, Inc., a Delaware corporation and successor-in-interest to Denali Concrete Management, Inc., a Nevada corporation, or OphthaliX, whose common shares are traded in the United States on OTC under the symbol "OPLI." In the spin-off transactions, we granted an exclusive license for the use of our CF101 drug candidate in the ophthalmic field to Eye-Fite Ltd., an Israel limited company and a former wholly-owned subsidiary of ours, or Eye-Fite, and transferred our issued and outstanding ordinary shares in Eye-Fite to OphthaliX in exchange for an 86.7% interest in OphthaliX. In connection with the spin-off transactions, OphthaliX completed a series of private placement financing transactions. Following the spin-off transactions and the private placement financing transactions, we held approximately 82% interest in OphthaliX and OphthaliX continues to develop the CF101 drug candidate for certain ophthalmic indications. See "Item 10. Additional Information—Material Contracts—OphthaliX Agreements."

Our capital expenditures for the years ended December 31, 2014, 2013 and 2012 were NIS 37,000, NIS 43,000 and NIS 17,000, respectively. Our current capital expenditures are made solely within Israel and primarily consist of the acquisition of computers and related communications equipment. Such capital expenditures are financed internally.

We qualify as an "emerging growth company," as defined in the JOBS Act. For as long as we are deemed an emerging growth company, we may take advantage of specified reduced reporting and other regulatory requirements that are generally unavailable to other public companies. These provisions include:

- an exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting required by Section 404 of the Sarbanes-Oxley Act of 2002;
- an exemption from compliance with any new requirements adopted by the PCAOB requiring mandatory audit firm rotation or a supplement to the auditor's report in which the auditor would be required to provide additional information about our audit and our financial statements; and
- reduced disclosure about our executive compensation arrangements.

We will continue to be deemed an emerging growth company until the earliest of:

- the last day of our fiscal year in which we have total annual gross revenues of $1,000,000,000 (as such amount is indexed for inflation every five years by the SEC to reflect the change in the Consumer Price Index for All Urban Consumers published by the Bureau of Labor Statistics, setting the threshold to the nearest $1,000,000) or more;
- the last day of our fiscal year following the fifth anniversary of the date of our first sale of common equity securities pursuant to an effective registration statement under the Securities Act;
- the date on which we have, during the prior three-year period, issued more than $1,000,000,000 in non-convertible debt; or
- the date on which we are deemed to be a 'large accelerated filer," as defined in Regulation S-K under the Securities Act.

B. Business Overview

We are a clinical-stage biopharmaceutical company focused on developing orally bioavailable small molecule therapeutic products for the treatment of autoimmune-inflammatory, oncological and ophthalmic diseases. Our platform technology utilizes the Gi protein associated A3AR as a therapeutic target. A3AR is highly expressed in inflammatory and cancer cells, and not significantly expressed in normal cells, suggesting that the receptor could be a unique target for pharmacological intervention. Our pipeline of drug candidates are synthetic, highly specific agonists and allosteric modulators, or ligands or molecules that initiate molecular events when binding with target proteins, targeting the A3AR.

Our product pipeline is based on the research of Dr. Pnina Fishman, who investigated a clinical observation that tumor metastasis can be found in most body tissues, but are rarely found in muscle tissue, which constitutes approximately 60% of human body weight. Dr. Fishman's research revealed that one reason that striated muscle tissue is resistant to tumor metastasis is that muscle cells release small molecules which bind with high selectivity to the A3AR. As part of her research, Dr. Fishman also discovered that A3ARs have significant expression in tumor and inflammatory cells, whereas normal cells have low or no expression of this receptor. The A3AR agonists and allosteric modulators, currently our pipeline of drug candidates, bind with high selectivity and affinity to the A3ARs and upon binding to the receptor initiate down-stream signal transduction pathways resulting in apoptosis, or programmed cell death, of tumors and inflammatory cells and to the inhibition of inflammatory cytokines. Cytokines are proteins produced by cells that interact with cells of the immune system in order to regulate the body's response to disease and infection. Overproduction or inappropriate production of certain cytokines by the body can result in disease. We have in-licensed certain patents and patent applications protecting three different A3AR ligands which represent our current pipeline of drug candidates under development and include two synthetic A3AR agonists, CF101 (known generically as IB-MECA) and CF102 (known generically as CI-IB-MECA) from the NIH, and an allosteric modulator at the A3AR, CF602 from Leiden University. In addition, we have out-licensed CF101 for (i) the treatment of autoimmune diseases to Seikagaku Corporation, a Japanese public corporation, or SKK, for the Japanese market, (ii) for the treatment of rheumatoid arthritis, or RA to Kwang Dong Pharmaceutical Co. Ltd., a South Korean limited company, or KD, for the Korean market and (iii) for the treatment of ophthalmic diseases to Eye-Fite, a wholly-owned subsidiary of OphthaliX for the global market. We also recently entered into a distribution agreement with Cipher Pharmaceuticals, Inc. for the distribution of CF101 for the treatment of psoriasis and rheumatoid arthritis in the Canadian market upon receipt of regulatory approvals.

Our product candidates, CF101, CF102 and CF602 are being developed to treat several autoimmune-inflammatory, oncological and ophthalmic indications. CF101 is in various stages of clinical development for the treatment of autoimmune-inflammatory diseases, including RA; psoriasis and osteoarthritis, or OA. CF101 is also being developed by OphthaliX for the treatment of ophthalmic indications, including glaucoma and uveitis. CF602 is our second generation allosteric drug candidate for the treatment of inflammatory diseases, which has shown proof of concept in in vitro and in vivo studies. The CF102 drug candidate is being developed for the treatment of HCC, and for the treatment of HCV.In addition, we recently announced that we are planning to develop CF602 to treat sexual dysfunction. Preclinical studies revealed that our drug candidates have potential to treat additional inflammatory diseases, such as Crohn's disease, oncological diseases and viral diseases, such as the JC virus, a virus that causes a potentially fatal brain disease in persons with an immunodeficiency.

We believe our pipeline of drug candidates represent a significant market opportunity. For instance, according to Visiongain, the world RA market size is predicted to generate revenues of $38.5 billion in 2017. According to GlobalData, the psoriasis drug market is forecasted to grow from $3.6 billion in 2010 to $6.7 billion by 2018. According to Global Industry Analysts, the global liver cancer drug market is expected to exceed $2 billion by 2015. GlobalData estimated the glaucoma market to exceed $3 billion by 2018.

We believe that our drug candidates have certain unique characteristics and advantages over drugs currently available on the market and under development to treat these indications. To date, we have generated our pipeline by in-licensing, researching and developing two synthetic A3AR agonists, CF101 and CF102, and an allosteric modulator, CF602. For example, our technology platform is based on the finding that the A3AR is highly expressed in pathological cells, such as various tumor cell types and inflammatory cells. High A3AR expression levels are also found in peripheral blood mononuclear cells, or PBMCs, of patients with cancer, inflammatory and viral diseases. PBMCs are a critical part of the immune system required to fight infection. We believe that targeting the A3AR with synthetic and highly selective A3AR agonists, such as CF101 and CF102, and allosteric modulators, such as CF602, induces anti-cancer and anti-inflammatory effects. In addition, our human clinical data suggests that the A3AR is a biological marker and that high A3AR expression prior to treatment may be predictive of good patient response to our drug treatment. In fact, as a result of our research we have developed a simple blood assay to test for A3AR expression as a predictive biological marker. We have been granted a U.S. patent with respect to the intellectual property related to such assay and utilized this assay in our Phase IIb study of CF101 tor the treatment of RA.

Moreover, we believe characteristics of CF101, as exhibited in our clinical studies to date, including its good safety profile, clinical activity, simple and less frequent delivery through oral administration and its low cost of production, position it well against the competition in the autoimmune-inflammatory markets, including the RA and psoriasis markets, where treatments, when available, often include injectable drugs, many of which can be highly toxic, expensive and not always effective. Furthermore, pre-clinical pharmacology studies in different experimental animal models of arthritis revealed that CF101 acts as a disease modifying anti-rheumatic drug, or a DMARD, which, when coupled with its good safety profile, make it competitive in the psoriasis, RA and OA markets. Our recent findings also demonstrate that a biological predictive marker can be utilized prior to treatment with CF101, which may allow it to be used as a personalized medicine therapeutic approach for the treatment of RA. We also believe CF101 is well-positioned against some of the competition in the ophthalmic markets, in particular, glaucoma, where treatments, when available, often include frequent self-administered eye drops, which may be more difficult than taking pills and may result in less than the full dose of the drug actually entering the eye, have undesirable side effects and do not simultaneously treat the underlying cause and relieve the symptoms associated with the indication. Like CF101, CF102 has a good safety profile, is orally administered and has a low cost of production, which we believe positions it well in the HCC market, where only one drug, Nexavar, has been approved by the FDA.

Nevertheless, other drugs on the market, new drugs under development (including drugs that are in more advanced stages of development in comparison to our drug candidates) and additional drugs that were originally intended for other purposes, but were found effective for purposes targeted by us, may all be competitive to the current drugs in our pipeline. In fact, some of these drugs are well established and accepted among patients and physicians in their respective markets, are orally bioavailable, can be efficiently produced and marketed, and are relatively safe. None of our product candidates have been approved for sale or marketing and, to date, there have been no commercial sales of any of our product candidates.

Our research further suggests that A3AR affects pathological and normal cells differently. While specific A3AR agonists, such as CF101 and CF102, and allosteric modulators, such as CF602, appear to inhibit growth and induce apoptosis of cancer and inflammatory cells, normal cells are refractory, or unresponsive to the effects of these drugs. To date, the A3AR agonists have had a positive safety profile as a result of this differential effect.

We also seek to obtain technologies that complement and expand our existing technology base by entering into license agreements with academic institutions and biotechnology companies. To date, we have in-licensed intellectual property which protects certain small molecules, such as CF101 and CF102, from the NIH, and CF602 from Leiden University. Under our license agreements we are generally obligated to diligently pursue product development, make development milestone payments, pay royalties on any product sale and make payments upon the grant of sublicense rights. The scope of payments we are required to make under our in-licensing agreements is comprised of various components that are paid commensurate with the progressive development and commercialization of our drug products. See “Item 4. Information on the Company—Business Overview—In-Licensing Agreements.”

In addition to in-licensing, we have also out-licensed one of our molecules to third-parties to capitalize on the experience, capabilities and location of such third-parties. Similar to our obligations under any in-license agreements, pursuant to these out-licensing agreements, our licensees are generally obligated to diligently pursue product development, make up-front payments, make development milestone payments and pay royalties on sales. Accordingly, we expect to fund certain of our future operations through out-licensing arrangements with respect to our product candidates. To date, we have out-licensed CF101 for the treatment of autoimmune diseases for the Japanese market to SKK, and CF101 for the treatment of RA for the Korean market to KD and CF101 for ophthalmic diseases for the global market to OphthaliX. See “Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements.”

We are currently: (i) expecting top-line results for a recently completed Phase II/III trial with respect to the development of CF101 for the treatment of psoriasis; (ii) preparing for a Phase III trial with respect to the development of CF101 for the treatment of RA; (iii) preparing for a Phase II study with respect to the development of CF101 for the treatment of OA; (iv) conducting a Phase II study with respect to the development of CF102 for the treatment of HCC (and as part of this study, we will also test CF102 in patients with both HCC and HCV); and (v) preparing for further preclinical work with respect to the development of CF602. OphthaliX is currently: (i) conducting a Phase II trial with respect to the development of CF101 for the treatment of glaucoma or related syndromes of ocular hypertension; and (ii) initiating a Phase II study of CF101 for the treatment of uveitis.

Our Strategy

Our strategy is to build a fully integrated biotechnology company that discovers, in-licenses and develops an innovative and effective small molecule drug portfolio of ligands that bind to a specific therapeutic target for the treatment of autoimmune-inflammatory, oncological, ophthalmic diseases and more. We continue to develop and test our existing pipeline, while also testing other indications for our existing drugs and examining, from time to time, the potential of other small molecules that may fit our platform technology of utilizing small molecules to target the A3AR. We generally focus on drugs with global market potential and we seek to create global partnerships to effectively assist us in developing our portfolio and to market our products. Our approach allows us to:

- continue to advance our clinical and preclinical pipeline;
- test our products for additional indications which fit our molecules' mechanism of action;
- identify other small molecule drugs or ligands;
- focus on our product candidates closest to realizing their potential; and
- avoid dependency on a small number of small molecules and indications.

Using this approach, we have successfully advanced our product candidates for a number of indications into various stages of clinical development. Specific elements of our current strategy include the following:

Successful development of our existing portfolio of small molecule orally bioavailable drugs for the treatment of various diseases. We intend to continue to develop our existing portfolio of small molecule orally bioavailable drugs, both for existing targeted diseases, as well as other potential indications. Our drug development will continue to focus on inflammatory, oncological and ophthalmic diseases. We will focus most prominently on advancing our product candidates that are in the most advanced stages, i.e., plaque psoriasis and RA (and later posterior uveitis and glaucoma) with respect to CF101, and HCC with respect to CF102. Following the announcement of top-line results that CF101 did not meet the dry eye syndrome or DES Phase III primary and secondary efficacy end-points, Ophthalix decided to end the development of CF101 for DES.

Use our expertise with our platform technology to evaluate in-licensing opportunities. We continuously seek attractive product candidates and innovative technologies to in-license or acquire. We intend to focus on product candidates that would be synergistic with our A3AR expertise. We believe that by pursuing selective acquisitions of technologies in businesses that complement our own, we will be able to enhance our competitiveness and strengthen our market position. We intend to utilize our expertise in A3AR and our pharmacological expertise to validate new classes of small molecule orally bioavailable drugs. We will then seek to grow our product candidate portfolio by attempting to in-license those various candidates and to develop them for a variety of indications.

Primarily develop products that target major global markets. Our existing product candidates are almost all directed at diseases that have major global markets. Our intent is to continue to develop products that target diseases that affect significant populations using our platform technology. We believe these arrangements will allow us to share the high development cost, minimize the risk of failure and enjoy our partners' marketing capabilities, while also enabling us to treat a more significant number of persons. We believe further that this strategy will increase the likelihood of advancing clinical development and potential commercialization of our product candidates.

Commercialize our product candidates through out-licensing and distribution arrangements. We have entered into two out-licensing arrangements with major pharmaceutical companies in the Far East and one distribution agreement with a growing pharmaceutical company in Canada. We intend to continue to commercialize our product candidates through out-licensing and distribution arrangements with third parties who may perform any or all of the following tasks: completing development, securing regulatory approvals, manufacturing, marketing and sales. We do not intend to develop our own manufacturing facilities or sales forces. If appropriate, we may enter into co-development and similar arrangements with respect to any product candidate with third parties or commercialize a product candidate ourselves. We believe these arrangements will allow us to share the high development cost, minimize the risk of failure and enjoy our partners' marketing capabilities. We believe further that this strategy will increase the likelihood of advancing clinical development and potential commercialization of our product candidates.

Our Product Pipeline

The table below sets forth our current pipeline of product candidates, including the target indication and status of each.

Clinical Application/Drug	Pre-Clinical	Phase I	Phase II	Phase III
Autoimmune-Inflammatory				
Psoriasis – CF101[(1)]				
Rheumatoid Arthritis – CF101[(2)]				
Osteoarthritis – CF101[(3)]				
Inflammation and Sexual Dysfunction – CF602[(4)]				
Oncology				
HCC – CF102[(5)]				
Ophthalmology[(6)]				
Glaucoma – CF101[(7)]				
Uveitis – CF101[(8)]				


Completed


On-going


Preparatory work

(1) We are expecting top-line results for a recently completed Phase II/III trial with respect to the development of CF101 for the treatment of psoriasis.
(2) We are preparing for a Phase III trial with respect to the development of CF101 for the treatment of RA.
(3) We are preparing for a Phase II study with respect to the development of CF101 for the treatment of OA.
(4) We are preparing for further preclinical work with respect to the development of CF602.
(5) We are conducting a Phase II study with respect to the development of CF102 for the treatment of HCC (and as part of this study, we will also test CF102 in patients with both HCC and HCV).
(6) OphthaliX, an 82% owned subsidiary of ours, develops CF101 for ophthalmic indications.
(7) OphthaliX is conducting a Phase II trial with respect to the development of CF101 for the treatment of glaucoma or related syndromes of ocular hypertension.
(8) OphthaliX is initiating a Phase II study of CF101 for the treatment of uveitis.

CF101

CF101, our lead therapeutic product candidate, is in development for the treatment of autoimmune-inflammatory diseases, psoriasis, RA and OA, and the ophthalmic diseases, glaucoma and uveitis. In certain of our pharmacological studies, CF101 has also shown potential for development for the treatment of Crohn's disease. CF101 is a highly-selective, orally bioavailable small molecule synthetic drug, which targets the A3AR. Based on our clinical studies to date, we believe that CF101 has a favorable safety profile and significant anti-inflammatory effects as a result of its capability to inhibit the production of inflammatory cytokines, such as TNF-α, IL-6 and IL-1, and chemokines, or small cytokines, such as MMPs, by signaling key proteins such as NF-κB and PKB/AKT. Overall, these up-stream events result in apoptosis of inflammatory cells. See Figure 1 below. CF101's anti-inflammatory effect is mediated via the A3AR, which is highly expressed in inflammatory cells.

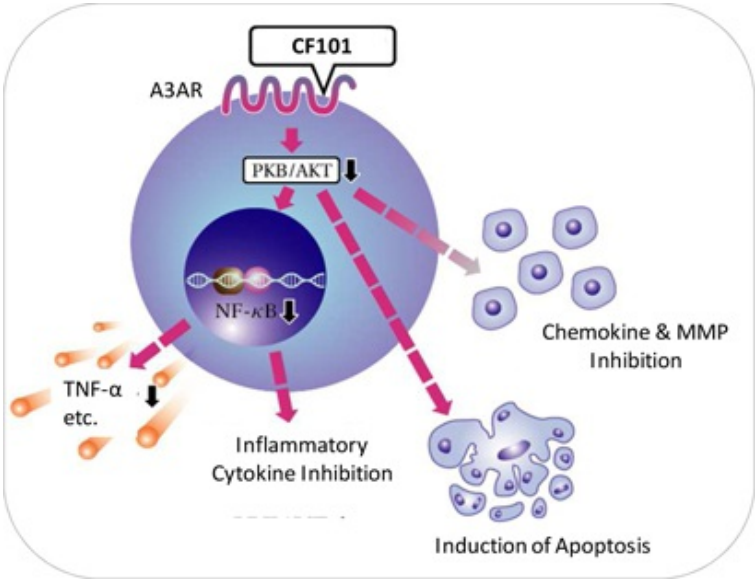


Figure 1: CF101 anti-inflammatory mechanism of action

Set forth below are general descriptions of the inflammatory and ophthalmic diseases with respect to which CF101 is currently undergoing, or is in preparation for clinical trials.

Psoriasis: Psoriasis is an autoimmune hereditary disease that affects the skin. In psoriasis, immune cells move from the dermis to the epidermis, where they stimulate keratinocytes, or skin cells, to proliferate. DNA acts as an inflammatory stimulus to stimulate receptors which produce cytokines, such as IL-1, IL-6, and TNF-α, and antimicrobial peptides. These cytokines and antimicrobial peptides signal more inflammatory cells to arrive and produce further inflammation. In other words, psoriasis occurs when the immune system overreacts and mistakes the skin cells as a pathogen, and sends out faulty signals that speed up the growth cycle of skin cells. Normally, skin cells grow gradually and flake off approximately every four weeks. New skin cells grow to replace the outer layers of the skin as they shed. But in psoriasis, new skin cells move rapidly to the surface of the skin in days rather than weeks. They build up and form thick patches called plaques.

There are five types of psoriasis: plaque, guttate, inverse, pustular and erythrodermic. The most common form, plaque psoriasis, is commonly seen as red and white hues of scaly patches appearing on the top first layer of the epidermis, or skin. In plaque psoriasis, skin rapidly accumulates at these sites, which gives it a silvery-white appearance. Plaques frequently occur on the skin of the lower back, elbows and knees, but can affect any area, including the scalp, palms of hands, soles of feet and genitals. The plaques range in size from small to large. In contrast to eczema, psoriasis is more likely to be found on the outer side of the joint. Some patients, though, have no dermatological symptoms.

Psoriasis is a chronic recurring condition that varies in severity from minor localized patches to complete body coverage. Fingernails and toenails are frequently affected, known as psoriatic nail dystrophy, and can be seen as an isolated symptom. Psoriasis can also cause inflammation of the joints, which is known as psoriatic arthritis.

Rheumatoid Arthritis: RA, is a chronic, systemic autoimmune-inflammatory disease that may affect many tissues and organs, but principally attacks flexible synovial, or joints, on both sides of the body. This symmetry helps distinguish RA from other types of arthritis, which is the general term for joint inflammation. Although the cause of RA is unknown, autoimmunity plays a pivotal role in both its chronicity and progression. The disease involves abnormal B cell–T cell interaction, which results in the release of cytokines. The cytokines signal the release of inflammatory cells. The inflammatory cells migrate from the blood into the joints and joint-lining tissue. There, the cells produce inflammatory substances that cause irritation, wearing down of cartilage, or the cushioning material at the end of bones, swelling and inflammation of the joint lining, which is caused by excess synovial fluid, the development of pannus, or fibrous tissue, in the joint, and ankylosis, or fusion of the joints. Joint inflammation is characterized by redness, warmth, swelling and pain within the joint. As the cartilage wears down, the space between the bones narrows. If the condition worsens, the bones could rub against each other. As the lining expands due to inflammation from excess fluid, it may erode the adjacent bone, resulting in bone damage. RA can also produce diffuse inflammation in the lungs, membrane around the heart, the membranes of the lungs, and white of the eye, and also nodular lesions, most common in subcutaneous tissue.

Osteoarthritis: OA is a common chronic degenerative joint disease that is characterized by a group of mechanical abnormalities involving degradation of joints, including articular cartilage, or the cartilage found on joint surfaces. Although degeneration of joint cartilage is the central feature in OA, the disease is also associated with changes in synovium and subchondral bone metabolism, causing inflammation of the synovial membrane in the involved joints. Synovial inflammation and local concentration of pro-inflammatory mediators seem to be directly involved in the generation of pain in osteoarthritic joints.

OA is related to, but not caused by, aging. As a person ages, the water content of the cartilage decreases, causing the cartilage to be less resilient. When the cartilage is less resilient, it can become susceptible to degradation or exacerbation of existing degeneration. Inflammation of the surrounding joint capsule can also occur, though often mild (compared to what occurs in RA). This can happen as breakdown products from the cartilage are released into the synovial space and the cells lining the joint attempt to remove them. New bone outgrowths, called “spurs” or osteophytes, can form on the margins of the joints. These bone changes, together with the inflammation, can be both painful and debilitating.

Mechanical stress on joints underlies all OA. There are many and varied sources of mechanical stress, including misalignments of bones caused by congenital or pathogenic causes, mechanical injury, obesity, loss of strength in muscles supporting joints and impairment of peripheral nerves, leading to sudden or uncoordinated movements that overstress joints. However, despite the numerous causes of osteoarthritis, the resulting pathology remains the same.

Glaucoma: Glaucoma is an eye disease in which the optic nerve is damaged. This optic nerve damage involves loss of retinal ganglion cells, or neurons located near the inner surface of the retina, in a characteristic pattern. There are many different subtypes of glaucoma, but they can all be considered to be a type of optic neuropathy. Raised intraocular pressure, or IOP, is the most important and only modifiable risk factor for glaucoma. However, some individuals may have high IOP for years and never develop optic nerve damage. This is known as ocular hypertension. Others may develop optic nerve damage at a relatively low IOP, and, thus, glaucoma. Untreated glaucoma can lead to permanent damage of the optic nerve and resultant visual field loss, which over time can progress to blindness.

Glaucoma can be roughly divided into two main categories, “open angle” and “closed angle” glaucoma. The angle refers to the area between the iris and cornea through which fluid must flow to exit the eye. The difficulty or inability of such fluid to exit the eye causes an acute increase of pressure and pain. Closed angle glaucoma can appear suddenly, is often painful and visual loss can progress quickly. However, the discomfort often leads patients to seek medical attention before permanent damage occurs. Open angle, chronic glaucoma tends to progress at a slower rate and patients may not notice they have lost vision until the disease has progressed significantly.

Uveitis: Uveitis is inflammation of the middle layer of the eye, or the uvea, caused by an immune reaction. Uveitis can be associated with auto-immune inflammatory diseases and various eye infections. Uveitis is a common cause of blindness. The most common form of uveitis is anterior uveitis, which involves inflammation in the front part of the eye. It is often called iritis because it usually only affects the iris, the colored part of the eye. The inflammation may be associated with autoimmune diseases, but most cases occur in healthy people. The disorder may affect only one eye and is most common in young and middle-aged people.

Posterior uveitis affects the back part of the uvea, and involves primarily the choroid, a layer of blood vessels and connective tissue in the middle part of the eye. This type of uveitis is called choroiditis. If the retina is also involved, it is called chorioretinitis. Anterior uveitis affects the front part of the uvea, and involves primarily the iris and the cilliary body. This type of uveitis is called iridocyclitis. These conditions may develop as a result of a body-wide, or systemic, infection or an autoimmune disease. Another form of uveitis is pars planitis. This inflammation affects the narrowed area, or the pars plana, between the iris, or colored part of the eye, and the choroid. Pars planitis usually occurs in young men and is generally not associated with any other disease. However, some evidence suggests it may be linked to Crohn's disease and, possibly, multiple sclerosis.

Pre-Clinical Studies of CF101

The information below is based on the various studies conducted with CF101, including preclinical studies. All of the studies were conducted by Can-Fite and/or by Can-Fite's partners or affiliates.

Pre-clinical studies are a set of experiments carried out in animals to show that a certain drug does not evoke toxicity. Based on the animal studies and safety data, one can approach the FDA and request permission to conduct a Phase I study in human beings.

The toxicity of CF101 has been evaluated following 28-day, 90-day, six-month and nine-month good laboratory practice repeated-dose toxicity studies in male and female mice (28-day, 90-day and six-month), dogs (single-dose only), and monkeys (28-day, 90-day and nine-month). Even though the dose of CF101 in these studies was escalated to an exposure that is many folds higher than the dose used in human clinical studies, no toxic side effects were identified.

Effects on cardiovascular parameters were evaluated in conscious instrumented monkeys and anesthetized dogs. These studies demonstrated no significant cardiovascular risk.

Genotoxicity studies were conducted in bacterial and mammalian mutation assays *in vitro* (i.e., laboratory) and in an *in vivo* (i.e., animal) mouse micronucleus assay. These studies were all negative, indicating no deleterious action on cellular genetic material.

Reproductive toxicology studies that we completed in mice and rabbits did not reveal evidence of negative effects on male or female fertility. In mouse teratology studies, or studies for abnormalities of physiological developments, craniofacial and skeletal abnormalities were observed at doses greater than 10 mg/kg; however, no such effects were observed at 3 mg/kg demonstrating the safety of the drug in this concentration range. Teratogenicity, or any developmental anomaly in a fetus, was not observed in rabbits given doses (greater than 13 mg/kg) that induced severe maternal toxicity in such rabbits.

Studies of P450 enzymes, or enzymes that participate in the metabolism of drugs, showed that CF101 caused no P450 enzyme inhibition, or increased drug activity, or induction, or reduced drug activity. Studies carried out with radiolabeled (C^{14}) CF101 in rats showed that the drug is excreted essentially unchanged. These studies also showed that the drug is widely distributed in all body parts, except the central nervous system.

Clinical Studies of CF101

The information below is based on the various studies conducted with CF101, including clinical studies in patients with autoimmune-inflammatory and ophthalmic diseases. All of the studies were conducted by Can-Fite and/or by Can-Fite's partners or affiliates.

Phase I Clinical Studies of CF101

CF101 has been studied comprehensively in normal volunteer trials to assess safety, pharmacokinetic metabolism and food interaction. Two Phase I studies in 40 healthy volunteers, single dose and repeated dose, indicated that CF101 is rapidly absorbed (reaching a maximal concentration within one to two hours) with a half-life of eight to nine hours. Some mild adverse events (principally, increased heart rate) were observed at doses higher than single doses of 10.0 mg and twice-daily doses of 5.0 mg. Such increase in heart rate was not accompanied by any change in QT intervals. The drug showed linear kinetics, in that the concentration that results from the dose is proportional to the dose and the rate of elimination of the drug is proportional to the concentration, and low inter-subject variability, meaning that the same dose of the drug does not produce large differences in pharmacological responses in different individuals. A fed-fast Phase I study (with and without food) demonstrated that food causes some attenuation in CF101 absorption; accordingly CF101 is administered to patients on an empty stomach in our trials. An additional Phase I study of the absorption, metabolism, excretion and mass balance of 4.0 mg (C^{14}) CF101 was conducted in six healthy male subjects and demonstrated that CF101 was generally well-tolerated in this group.

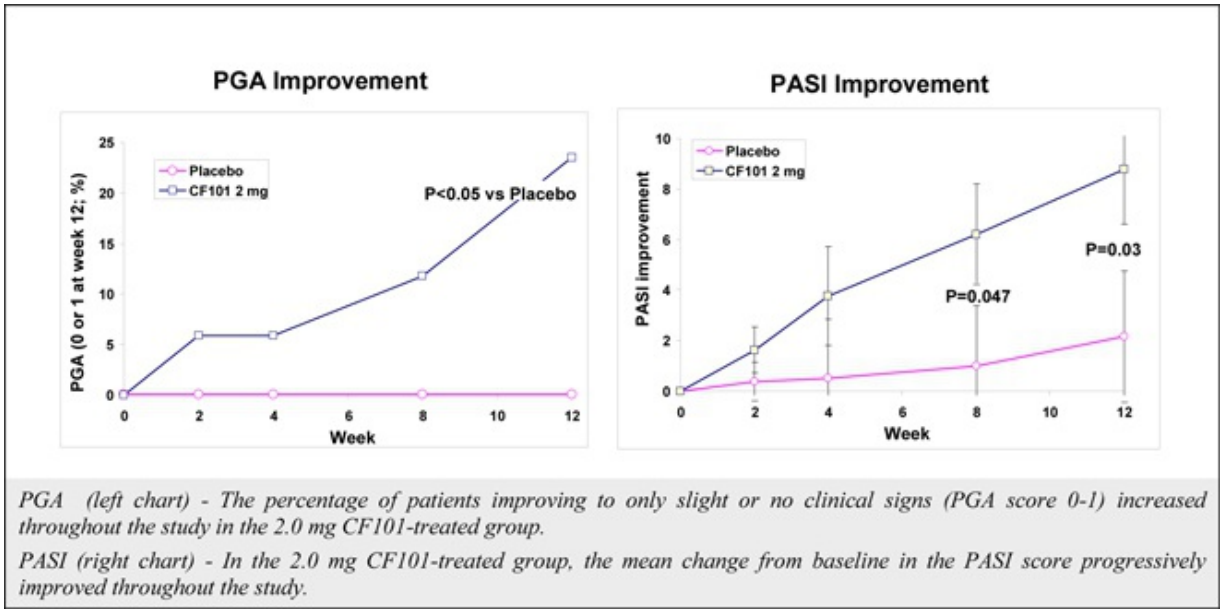
Based on the findings from Phase I clinical studies, 4.0 mg BID, or twice daily, was selected as the upper limit for initial Phase II clinical trials.

Phase II and Phase II/III Clinical Studies of CF101

CF101 has completed 16 Phase I, II and III studies in Psoriasis, RA and DES in approximately 1,410 patients (1,000 patients treated with CF101 and 410 patients treated with a placebo) for an aggregate exposure of approximately 250 patient years (for the patients treated with CF101). These studies indicate that CF101 has a favorable safety profile at doses up to 4.0 mg BID for up to 12 weeks. In the Phase II and III studies, we did not observe a dose-response relationship between CF101 and adverse events. Moreover, we did not observe any clinically significant changes in vital signs, electrocardiograms, blood chemistry or hematology. CF101 given as a standalone therapy reached the primary endpoint in Phase II clinical studies in psoriasis and DES. In addition, we observed positive data utilizing CF101 as a standalone drug in a Phase IIa clinical study in RA. In this study, we also observed a significant direct correlation between A3AR expression prior to treatment and the patients' responses to CF101. However, we did not fully attain the primary endpoint in this study as we did not observe a significant difference in responses between CF101 and the placebo (which for this study was 0.1 mg of CF101). Moreover, two Phase IIb studies in RA utilizing CF101 in combination with methotrexate, a generic drug commonly used for treating RA patients, or MTX, also failed to reach the primary endpoints. Based on this data, we believe that the failures in the Phase IIb studies in RA may have been due to low A3AR expression in the MTX-treated patients. A phase IIb of CF101 given as a standalone therapy in patients with A3AR expression levels above a certain threshold reached the primary endpoint in RA in December 2013. CF101 has been tested in Phase II trials to establish dose and activity (first, orally administered capsules and then tablets in formulations of 1.0, 2.0 and 4.0 mg of CF101 BID) in psoriasis (moderate to severe plaque psoriasis), RA and DES (moderate to severe.

Psoriasis: The rationale for utilizing CF101 to treat psoriasis stems from our pre-clinical pharmacology studies showing that CF101 acts as an anti-inflammatory agent via the inhibition of inflammatory cytokines, including TNF-α, which plays a major role in the pathogenesis of psoriasis. In addition, the A3AR is over-expressed in the tissue and PBMCs of patients with psoriasis.

We completed an exploratory Phase II trial in ten European and Israeli medical centers involving 76 patients. This study was a randomized, double-blind, placebo controlled and included four cohorts of 1.0, 2.0, and 4.0 mg of CF101 and a placebo for a 12-week period. The study objectives were efficacy and safety of daily doses of CF101 administered orally in patients with moderate-to-severe plaque-type psoriasis and the efficacy endpoints were improvements in both the Psoriasis Area Sensitivity Index score, or PASI score, and the Physicians' Global Assessment score, or PGA score. We concluded that CF101 met such efficacy endpoints and was safe, well tolerated and effective in ameliorating disease manifestations in these patients. The patient group receiving 2.0 mg CF101 BID showed progressive improvement over the course of the 12-week study in the PGA and PASI scores. Analysis of the mean change from baseline in the PASI score at week 12 revealed a statistically significant difference between the 2.0 mg CF101 BID treated group and the placebo group ($P < 0.001$ versus baseline and $P = 0.031$ versus placebo). Analysis of the PGA score revealed that 23.5% of the patients treated with the 2.0 mg CF101 BID achieved a score of 0 or 1, in comparison to 0% in the placebo group ($P < 0.05$). The study also demonstrated linear improvement in patients in both PASI and PGA. See Figure 2. No drug-related serious adverse events were evident during the study.

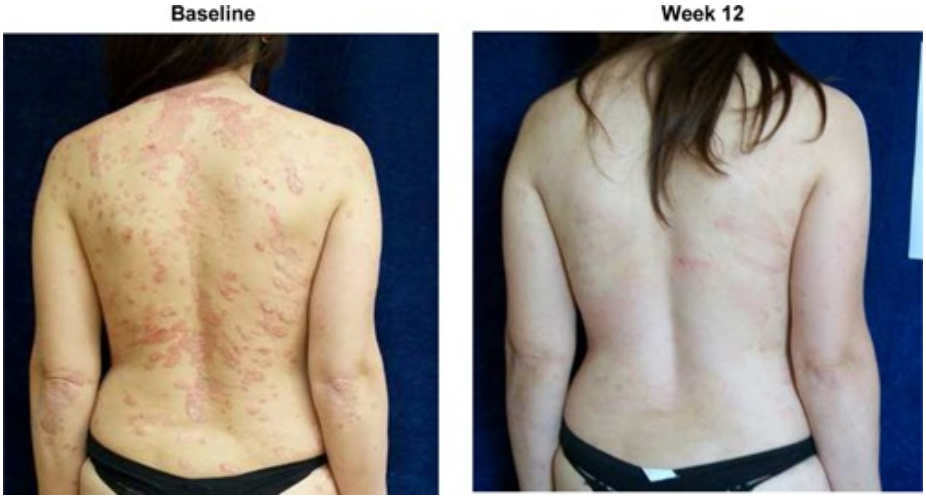


PGA (left chart) - The percentage of patients improving to only slight or no clinical signs (PGA score 0-1) increased throughout the study in the 2.0 mg CF101-treated group.

PASI (right chart) - In the 2.0 mg CF101-treated group, the mean change from baseline in the PASI score progressively improved throughout the study.

Figure 2: Psoriasis efficacy by PGA and PASI

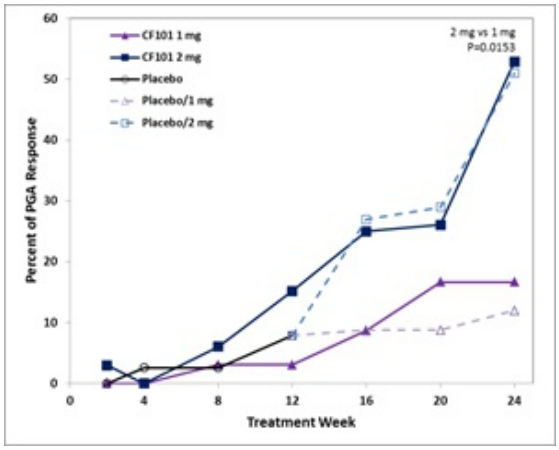
Set forth below are representative pictures of a patient with plaque-type psoriasis on the upper and lower back treated with 2.0 mg CF101 BID, both baseline and week 12.



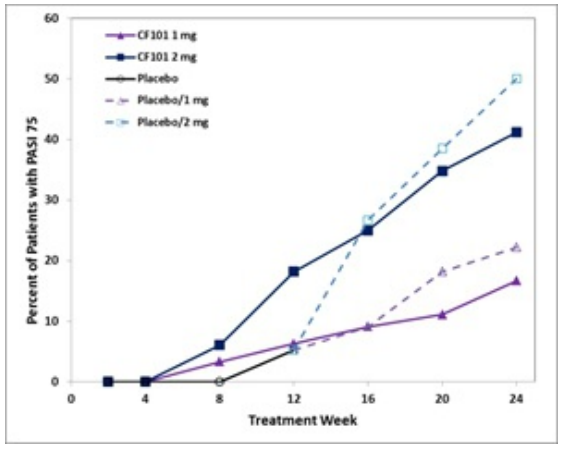
A comparison between baseline and week 12 of a patient treated with 2.0 mg CF 101

In February 2015, we completed a Phase II/III randomized, double-blind, placebo-controlled, dose-finding study of the efficacy and safety of CF101 administered daily orally in patients with moderate-to-severe plaque psoriasis. This clinical trial enrolled 326 patients in 17 clinical centers in the United States, Europe and Israel, of which 103 patients were enrolled in the first study cohort and were treated for 6 months and 223 patients were enrolled in the second study cohort and were treated for 8 months. The first study cohort was comprised of three arms with patients receiving: 1 mg of CF101; 2 mg of CF101; and placebo. All patients receiving placebo were switched to either 1 mg or 2 mg of CF101 after 12 weeks. Based on a positive safety and efficacy interim analysis of the first 103 patients who completed 24 weeks of treatment in the trial, we decided to continue patient enrollment for the second stage of the study and the study protocol was amended to extend the CF101 2.0 mg BID and placebo administration for a period of 32 weeks. The positive clinical effects of the CF101 2.0 mg BID dose relative to a placebo were observed in a variety of standard psoriasis assessment parameters, including PASI 75 and PGA scores, with the responses accumulating steadily over the 24-week treatment period. See Figure 3. We believe that this clinical data corroborates the published Phase II study results described above and confirms the dose selection, while the favorable safety profile of CF101 further supports its development for the systemic treatment of moderate-to-severe psoriasis. The topline results of our Phase II/III trial are expected to be released at the end of March 2015.

PGA Improvement



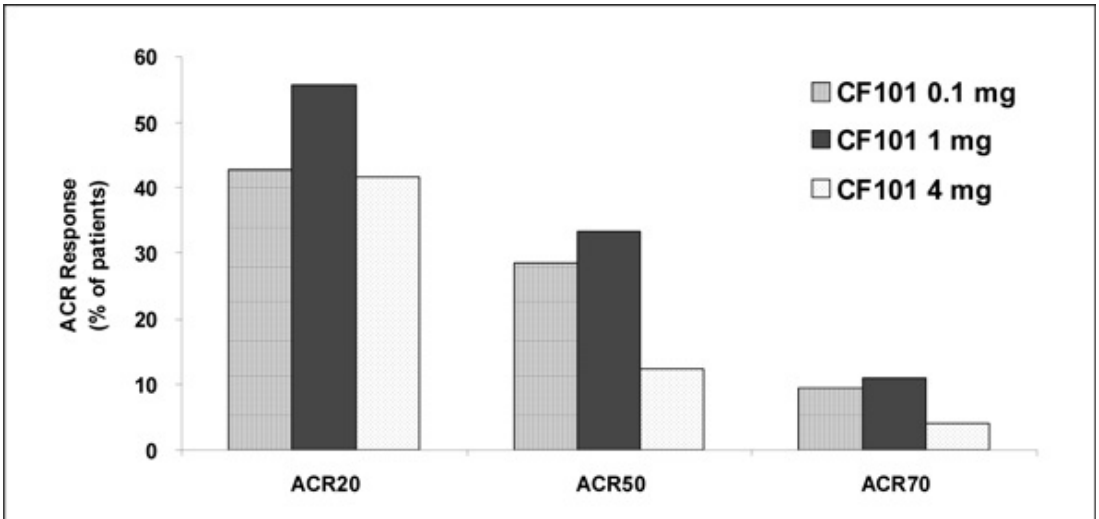
PASI Improvement



Interim data included 103 patients who were randomized to CF101 1mg, CF101 2mg and placebo and were treated for 24 weeks. On week 12 placebo were randomized to CF101 1mg or 2mg dose.PGA (left chart) - The percentage of patients presenting only slight or no clinical signs (PGA score 0-1) increased throughout the study period in the 2 mg CF101-treated group.PASI (right chart) - In the 2 mg CF101-treated group, a progressive improvement in the percentage of patients presenting PASI 75 improvement was observed.

Figure 3: Psoriasis efficacy by PGA and PASI

Rheumatoid Arthritis: We conducted a Phase IIa blinded to dose study in 74 patients with RA, randomized to receive CF101 as a monotherapy in one of three doses—0.1 mg, 1.0 mg and 4.0 mg. The primary efficacy endpoint was ACR20 response at week 12, a criterion determined by the American College of Rheumatology that reflects 20% improvement in inflammation parameters. The study data revealed maximal response at the 1.0 mg group, showing 55.6% with ACR20, 33.3% with 50% improvement, or ACR50, and 11.5% with 70% improvement, or ACR70. CF101 administered BID for 12 weeks resulted in improvement in signs and symptoms of RA and was safe and well-tolerated. See Figure 4. Studies in the United States were conducted pursuant to an open IND which was received by the FDA in 2005.



Percentages of rheumatoid arthritis patients who met the American College of Rheumatology, or ACR, criteria for 20%, 50% and 70% improvement (ACR20, ACR50 and ACR70, respectively) during treatment with 0.1 mg, 1.0 mg or 4.0 mg of CF101 twice daily for 12 weeks.

Figure 4: Rheumatoid Arthritis efficacy by ACR

Subsequently, two Phase IIb studies with CF101 in combination with MTX were conducted. The study protocols were multicenter, randomized, double-blind, placebo-controlled, parallel-group and dose-finding to determine the safety and efficacy of daily CF101 administered orally when added to weekly MTX in patients with active RA. The objectives of both studies were improvement in ACR20, ACR50, ACR70 and DAS28, or the Disease Activity Score of 28 Joints, and EULAR, or the European League Against Rheumatism, response criteria, as well as a positive safety profile. The trials' primary endpoints were both ACR20.

The first Phase IIb trial showed that the combined treatment had an excellent safety profile, but no significant ACR20 response was observed between the RA group treated with CF101 and MTX and the group treated with MTX alone (the placebo group). However, the ACR50, ACR70 and the EULAR Good Values in the combined treatment group were higher than those of the MTX placebo group. The study also indicated that the 1.0 mg CF101 dose was the most favorable dose, i.e., the dose yielded the highest ACR50 and EULAR Good Values as compared to the MTX placebo group. The most commonly reported adverse events in this study included nausea, dizziness, headache and common bacterial and viral infections and infestations.

Following a decision of our Clinical Advisory Board in October 2007, an additional Phase IIb study was initiated. This study was conducted in medical centers in Europe and Israel and included 230 patients who received the drug orally BID (0.1 and 1.0 mg CF101 tablets plus MTX versus a placebo, which was MTX alone) for 12 weeks. On April 30, 2009, we published preliminary results of the Phase IIb study, which were later confirmed as the final results, also indicating that the study's objectives were not achieved. The most commonly reported adverse events in this study included nausea, myalgia and dizziness.

The two Phase IIb studies failed to achieve the primary endpoint of ACR20. A cross study analysis of the three RA clinical studies revealed that in the first Phase IIa study, where CF101 had been administered as a standalone drug, A3AR had been over-expressed in the patients' PBMCs prior to CF101 treatment, whereas A3AR had not been over-expressed in the Phase IIb patient population. We believe, based on the foregoing data, that there may be a direct and statistically significant correlation between A3AR over-expression at baseline and patients' response to CF101, and that CF101 should be administered as a standalone drug and not in combination with MTX. Furthermore, the correlation between A3AR expression levels prior to treatment and patients' response to the drug suggest that the A3AR may be a predictive biomarker to be analyzed prior to CF101 treatment. See Figures 5 and 6.

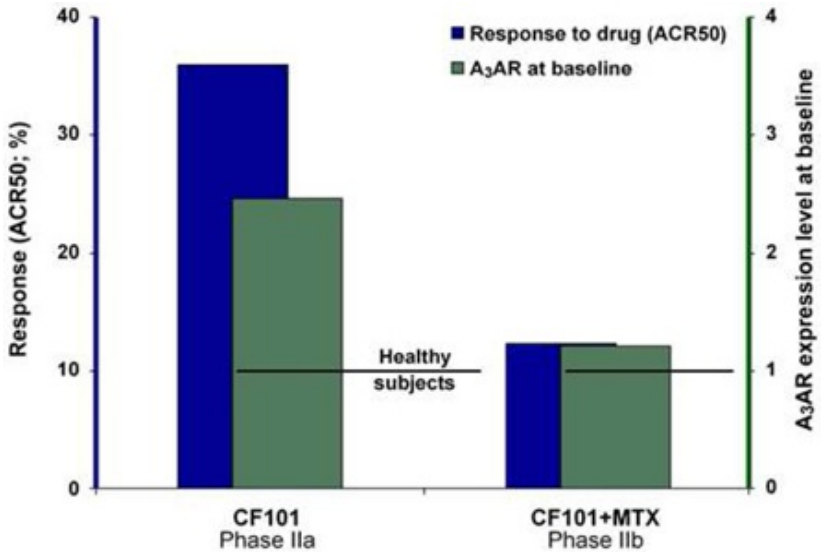


Figure 5: Direct correlation between A3AR at baseline and response to CF101

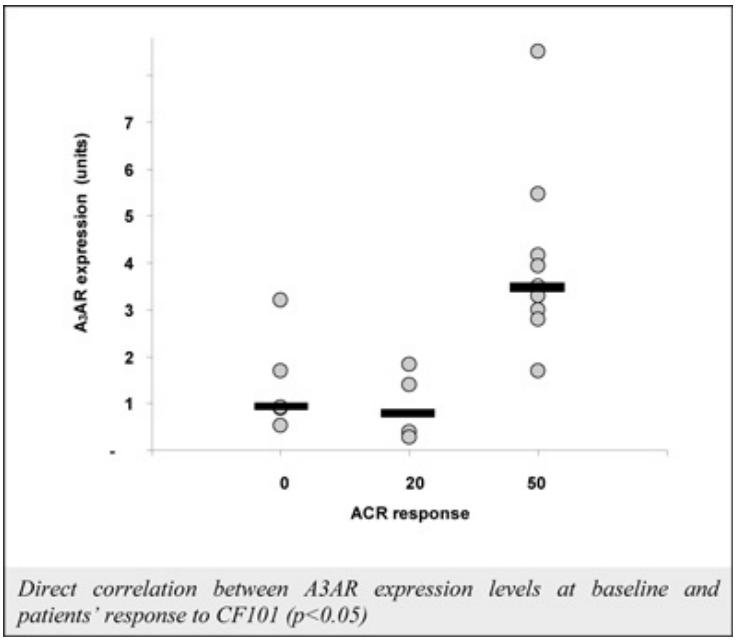


Figure 6: Direct correlation between A3AR at baseline and response to CF101

Based on the results of the two Phase IIb studies, we conducted an additional Phase IIb clinical study with CF101 as a stand-alone, monotherapy treatment and not in combination with MTX. The trial wasa 12-week multicenter, randomized, double-blind, placebo-controlled, parallel-group study involving 79 patients to determine the safety and efficacy of CF101 administered orally daily in patients with active RA and elevated baseline expression levels of the A3AR in PBMCs. Enrolled patients had high baseline A3AR biomarker expression (determined at 1.5-fold over a predetermined age-matched standard). This selection criteria was made following the findings during previous Phase IIa and IIb RA studies showing a positive correlation between A3AR expression at baseline and patients' response to the drug, potentially rendering A3AR expression as a predictive biomarker.The primary objectives of this study wereto determine the efficacy of oral CF101 when administered daily as a standalone treatment for 12 weeks to patients with active RA and elevated baseline expression levels of the A3AR in the patients' PBMCs, in comparison to a placebo treatment, and to assess the safety of daily oral CF101 under the circumstances of the trial. In December 2013, we announced the results of the study in which CF101 met all primary efficacy endpoints, showing statistically significant superiority over placebo in reducing signs and symptoms of RA as compared to the placebo. The treatment had an ACR20 response rate of 49% for CF101 compared to 25% for placebo (p=0.035), an ACR50 response rate of 19% for CF101 compared to 9% for placebo, and an ACR70 response rate of 11% for CF101 arm compared to 3% for placebo. Similar to our observations in the previously reported CF101 psoriasis trials, the response of patients with RA was cumulative over time, suggesting a consistent anti-inflammatory effect of CF101. Moreover, half of the RA patients treated with CF101 showed clinically meaningful improvement.CF101 was very well-tolerated and showed no evidence of immunosuppression, and there were no severe treatment-emergent adverse events during the study. A subgroup analysis of 16 patients with no prior systemic therapy showed a dramatic increase in the response showing ACR20 of 75%, ACR50 50%, and ACR70 50%. We believe this may be related to the fact that in this patient population there is a full receptor expression since they had not been treated earlier with any systemic drugs.

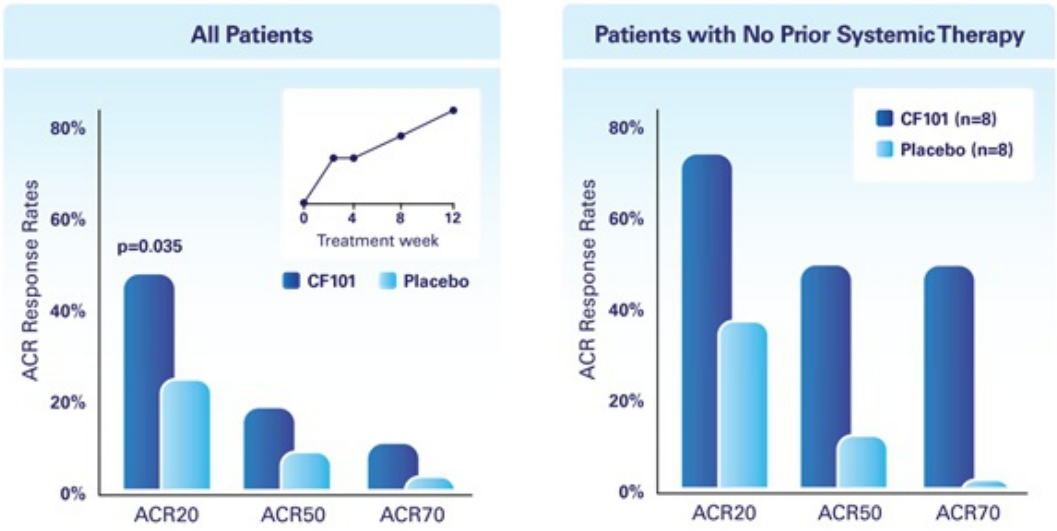


Figure 7: ACR response data –Rheumatoid Arthritis phase IIb

In December 2014, we completed the design of an RA Phase III study of CF101. The Phase III study will be a multicenter, randomized, double-blind, placebo-controlled, parallel-group study that will investigate the efficacy and safety of daily CF101 administered orally as a monotherapy for 12 weeks to patients with active RA. The study will have three arms, a 2 mg CF101 dose, a 3mg CF101 dose and placebo, given orally twice daily in the form of tablets. Approximately 300 patients are expected to be enrolled in the study, where sample size for each treatment group will be approximately 100 patients and will provide a statistical power of at least 90%. The study primary end point will be ACR 20 response at Week 12. The A3 adenosine receptor biomarker will be evaluated prior to treatment and its correlation to patients' response to the drug will be analyzed upon study conclusion.

DES: DES is an eye disease caused by eye dryness, which, in turn, is caused by either decreased tear production or increased tear film evaporation. A Phase II study in DES was conducted by Can-Fite after discovering that patients in the Phase IIa study for another condition also experienced improvement in DES symptoms. The results of the Phase II trial demonstrated the ability of CF101 to improve signs of ocular surface inflammation of the patients studied. Following positive results in the Phase II study, we initiated a Phase III DES trial, under an IND with the FDA which was conducted by OphthaliX in the United States, Europe and Israel.The randomized, double-masked Phase III clinical trial enrolled 237 patients with moderate-to-severe DES who were randomized to receive two oral doses of CF101 (0.1 and 1.0 mg) and a placebo, for a period of 24 weeks. The primary efficacy endpoint was complete clearing of corneal staining. In December 2013, we announced the results of this Phase III study of CF101 for the treatment of DES. In the study, CF101 did not meet the primary efficacy endpoint of complete clearing of corneal staining, nor the secondary efficacy endpoints. Nonetheless, CF101 was found to be well tolerated.In 2014 we decided to end the development of CF101 for the DES indication. This decision was based on a lack of correlation between patients' response to CF101 and over-expression of the drug target, the A3 adenosine receptor in this patient population.

Glaucoma: We believe that the statistically significant decrease in IOP in the Phase II trial for DES, although observed in subjects without ocular hypertension, is clinically significant and indicates that CF101 may also have potential as a glaucoma therapy, as the main goal of glaucoma therapy is to reduce IOP. This finding led to a patent application for the use of CF101 for lowering IOP. It is our belief that this result, together with the neuro-protective and anti-inflammatory effects that have been demonstrated in our studies and the studies of others, warrant rapid progression into clinical study in this indication. A Phase II study in patients with glaucoma or related syndromes of ocular hypertension is currently ongoing in Israel and Europe via OphthaliX. This study is a randomized, double-masked, placebo-controlled, parallel-group study of the safety and efficacy of daily CF101 administered orally in subjects with elevated IOP. The objective of this study are to determine the safety and efficacy of oral CF101 in lowering IOP when administered BID for 16 weeks in subjects with elevated IOP. OphthaliX has enrolled 44 subjects in the first segment of the study, randomized in a 3:1 ratio to CF101 1.0 mg treatment to the placebo. OphthaliX is currently in the process of enrolling approximately 44 subject to the second segment randomized in a 3:1 ratio to CF101 2.0 mg treatment to the placebo The full study data is expected to be announced in the second half of2015. Neither we nor OphthaliX has filed an IND for this indication as CF101 for the treatment of glaucoma is not currently being clinically tested in the United States and there are no near-term plans to do so.

Additional Developments with CF101

Uveitis

Former pre-clinical pharmacology studies conducted by us in collaboration with a worldwide leading laboratory in uveitis research at the National Eye Institute at the U.S National Institute of Health, or the NIH, under a Cooperative Research and Development Agreement, demonstrated that CF101 was effective in inhibiting the development of posterior uveitis in an experimental animal model. Additional preclinical studies conducted by OphthaliX, showed that CF101 was effective in treating anterior uveitis in experimental animal models.

The efficacy of CF101 in treating both anterior and posterior uveitis in experimental animal models supports further testing of CF101 for the treatment of patients with either anterior or posterior uveitis. We, together with the NIH, have applied for a patent for the use of CF101 for the treatment of uveitis. We have licensed our share of this intellectual property to OphthaliX and together with OphthaliX are in discussions with the NIH to obtain an exclusive license on the NIH's share of this intellectual property. OphthaliX submitted a protocol for a Phase II uveitis study in Europe and Israel to investigate the efficacy and safety of CF101 in 45 patients with active, sight-threatening, noninfectious intermediate or posterior uveitis, who will be treated with either CF101 or a placebo for a period of six months. The primary endpoint of this study is the proportion of subjects whose vitreous haze score improves by two or more grades on the "Miami Scale" (Vitreous Haze: Miami Scale 2). OphthaliX is currently reviewing its clinical development plans and intends to provide an update on the development for this indication on a later stage. Neither the OphthaliX nor we have filed an IND for this indication as CF101 for the treatment of uveitis is not currently being clinically tested in the United States and there are no near-term plans to do so.

Osteoarthritis

According to the Arthritis Foundation, OA is the most common arthritic disease. Currently, there is a shortage of effective drugs for treating OA patients. CF101 has induced a significant anti-inflammatory effect in experimental animal models with respect to the treatment of OA and, as such, we are currently preparing for a Phase II study. We have not yet filed an IND for this indication as CF101 for the treatment of OA is not currently being clinically tested in the United States and there are no near-term plans to do so.

Crohn's Disease

Crohn's disease is an inflammatory bowel disease that may affect any portion of the gastrointestinal tract, causing a wide variety of symptoms. It primarily causes abdominal pain, diarrhea, vomiting and weight loss, however, it may also cause complications outside the gastrointestinal tract, such as skin rashes, arthritis, inflammation of the eye, tiredness and lack of concentration. Pre-clinical pharmacology studies that we have conducted demonstrated the efficacy of CF101 for the treatment of Crohn's disease. We do not presently have plans for the treatment of Crohn's disease.

CF102

CF102 is our second drug candidate and is under development for the treatment of HCC and HCV. CF102 is also a small, orally bioavailable molecule, and an A3AR agonist, with high affinity and selectivity to the A3AR. In comparison to the expression in adjacent normal liver tissue, the A3AR is over-expressed in tumor tissues of patients with HCC, and the over-expression is also reflected in the patients' PBMCs. A3AR over-expression in the patients' tumor cells and PBMCs is attributed to high expression of certain A3AR transcription factors. The binding of CF102 to the A3AR results in down-regulation, or a decrease in the quantity of a cellular component, such as the number of receptors on a cell's surface, of certain A3AR transcription factors. Our studies have shown that this down-regulation leads to apoptosis of HCC cells. In our pre-clinical and clinical studies, CF102 demonstrated anti-cancer, anti-viral and liver protective effects. As a result, we believe that CF102 can be used to treat a variety of oncological and liver-related diseases and viruses. In February 2012, the FDA granted an orphan drug status for the active moiety, or the part of the drug that is responsible for the physiological or pharmacological action of the drug substance, of CF102 for the treatment of HCC. An orphan drug designation is a special designation by the FDA for drug approval and marketing. The special designation is granted to companies that develop a given drug for unique populations and for incurable and relatively rare diseases. The orphan drug designation program provides orphan status to drugs and biologics which are intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the United States. Orphan drug designations have enabled companies to achieve medical breakthroughs that may not have otherwise been achieved due to the economics of drug research and development as this status lessens some of the regulatory burdens, for approval, including statistical requirements for efficacy, safety and stability, in an effort to maintain development momentum. Orphan drug designation also results in additional marketing exclusivity and could result in certain financial incentives.

Set forth below are general descriptions of the diseases with respect to which CF102 has underwent or is currently undergoing clinical trials.

HCC: HCC is an oncological disease characterized by malignant tumors that grow on the surface or inside of the liver. This type of tumor is refractory to chemotherapy and to other anti-cancer agents. HCC, like any other cancer, develops when there is a mutation to the cellular machinery that causes the cell to replicate at a higher rate and/or results in the cell avoiding apoptosis. Chronic infections of Hepatitis B and/or C can aid the development of HCC by repeatedly causing the body's own immune system to attack the liver cells, some of which are infected by the virus. While this constant cycle of damage followed by repair can lead to mistakes during repair which in turn lead to carcinogenesis, this hypothesis is more applicable, at present, to HCV. Chronic HCV causes HCC through cirrhosis. In chronic Hepatitis B, however, the integration of the virus into infected cells can directly induce a non-cirrhotic liver to develop HCC. Alternatively, repeated consumption of large amounts of ethanol can have a similar effect.

Hepatitis C: HCV is an infectious disease affecting primarily the liver, caused by the Hepatitis C virus. The infection is often asymptomatic, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years, and chronic liver disease. The virus also increases the chance for HCC development. In some cases, those with cirrhosis will develop liver failure, liver cancer or life-threatening esophageal and gastric varices, or dilated submucosal veins, which can be life-threatening. HCV is spread primarily by blood-to-blood contact often associated with intravenous drug use, poorly sterilized medical equipment, transfusions, and sexual intercourse.

Pre-Clinical Studies of CF102

We conducted several pre-clinical studies, including studies of toxicity. The results indicated that CF102 was well- tolerated with no adverse effects. In these studies, we evaluated the toxicity, stability, metabolism and other safety parameters of CF102 at doses much higher than the doses that we currently administer to humans in our clinical trials of CF102. In pre-clinical pharmacology studies, CF102 inhibited the growth of HCC via the induction of tumor cell apoptosis. In addition, in collaboration with leading virology labs, we observed that CF102 inhibited viral replication of HCV through the down-regulation of viral proteins. Both of these findings served as a basis to further explore development of this drug for HCC and HCV. Moreover, our pre-clinical studies demonstrated that CF102 acted to stimulate liver regeneration after partial hepatectomy, or removal of a part of the liver, and as such, we applied for a patent for this treatment.

Clinical Studies of CF102

The information discussed below is based on the various studies conducted by Can-Fite with CF102, including clinical studies in patients with oncological and liver-related diseases and viruses.

Phase I Clinical Study

CF102 completed a Phase I double-blind, randomized, placebo-controlled, ascending single dose trial to evaluate the safety, tolerability, and pharmacokinetics of orally administered CF102 in healthy volunteers. The study was conducted in the United States under an open IND. CF102 was found to be safe and well-tolerated with a half-life time of 12 hours. See Figure 10.

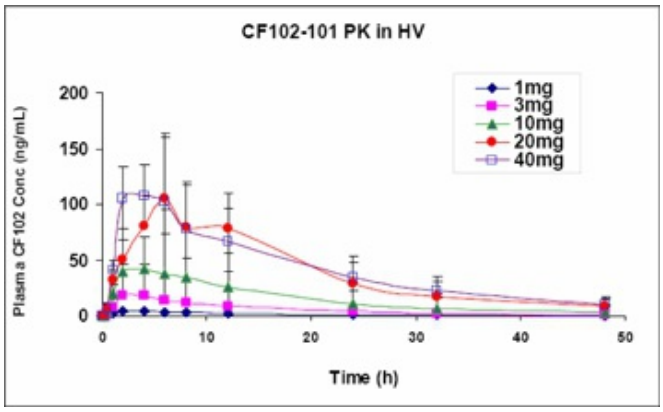


Figure 10. CF102 Pharmacokinetic profile

Phase I/II Clinical Study

CF102 completed two Phase I/II studies in Israel, one in patients with HCC and another in patients with HCV. The HCC Phase I/II study was an open-label, dose-escalation study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of orally administered CF102 in patients with advanced HCC. The primary objectives of the study were to determine the safety and tolerability, dose-limiting toxicities, maximum tolerated dose, and recommended Phase II dose of orally administered CF102 in patients with advanced HCC; and to assess the repeat-dose pharmacokinetics behavior of CF102 in those patients. The secondary objectives were to document any observed therapeutic effect of CF102 in patients with HCC and to evaluate the relationship between PBMCs and the A3AR expression at baseline, as a biomarker, and the effects of CF102 in patients with HCC. The study included 18 patients, nine of which were also carriers of HCV. The initial dose of CF102 was 1.0 mg BID, with planned dose escalations in subsequent cohorts to 5.0 and 25.0 mg BID. This Phase I/II study achieved its objectives, showing a good safety profile, or no material differences versus a placebo with respect to observed and patient-indicated side effects, for CF102 and a linear pharmacokinetic drug profile, with no dose-limiting toxicities at any dose level. The median overall survival time for the patients in this study was 7.8 months, which is encouraging data considering that (i) 67% of the patient population in the study had previously progressed on Nexavar, produced by Onyx Pharmaceuticals and Bayer, and that CF102 was a second line therapy for these patients and (ii) 28% of the patient population were Child-Pugh Class B patients (patients classified on the Child Pugh scoring system for chronic liver disease as having significantly impaired liver function) whose overall survival time is usually 3.5 to 5.5 months. Accordingly, we may also consider CF102 as a drug to be developed for this patient sub-population of Child-Pugh Class B patients. CF102 had no adverse effect on routine measures of liver function over a six-month period in 12 patients treated for at least that duration. These findings are consistent with our pre-clinical CF102 data which demonstrated a protective effect on normal liver tissue in an experimental model of liver inflammation. As such, CF102 may potentially be a safer alternative to patients with cirrhosis and/or hepatic impairment. The study also demonstrated a direct relationship between A3AR expression at baseline and patients' response to CF102, suggesting A3AR as a predictive biological marker. We also observed a decrease in the viral load of seven out of nine patients who were also carriers of HCV. The most commonly reported adverse events included loss of appetite, ascites, nausea, diarrhea, constipation and pain. However, many of these events are expected in a population of patients with advanced HCC. The most frequently reported drug-related adverse events included diarrhea, fatigue, loss of appetite, pain and weakness.

Our second Phase I/II study was a randomized, double-blind, placebo-controlled, dose-escalation study evaluating the safety, tolerability, biological activity, and pharmacokinetics of orally administered CF102 in 32 subjects with chronic HCV genotype 1. Eligible subjects were assigned in a 3:1 ratio (eight subjects in each cohort) to receive QD or BID treatment (1.0, 5.0 and 25.0 mg of CF102) for 15 days with oral CF102 or with a placebo. Dose escalation occurred in four sequential cohorts. The study's primary objectives were to determine the safety and tolerability of orally administered CF102 in patients with chronic HCV genotype 1, to assess the effects on HCV load during 15 days of treatment with CF102 and to assess the repeat-dose pharmacokinetic behavior of CF102 under the conditions of this trial. The secondary objective of this trial was to perform an exploratory evaluation of the relationship between A3AR in PBMCs at baseline and the clinical effects of CF102 on the study's patients. Following the decrease in HCV load that had been observed in HCV patients treated with CF102 in the parallel HCC study and the good safety profile of CF102, we received Israeli Institutional Review Board approval to extend the treatment period of the Phase I/II in patients with HCV to four months with the 1.0 mg dose vs. the placebo. The results of this Phase I/II HCV study demonstrated safety and a linear pharmacokinetic drug profile, however, no significant decrease in the viral load was observed. Notwithstanding, we did observe in the parallel HCC study that seven out of the nine patients with both HCC and HCV experienced a decrease in viral load and that these seven patients were treated with higher CF102 dosages than what was administered to the patients with chronic HCV genotype 1 only, and not HCC, possibly explaining the difference in results. The most commonly reported adverse events included loss of appetite, ascites, nausea, diarrhea, constipation and pain. However, many of these events are expected in a population of patients with advanced HCV. The most frequently reported drug-related adverse events included diarrhea, fatigue, loss of appetite, pain and weakness.

We are conducting a Phase II study in HCC patients. In January 2013, as part of our preparatory work for such study, we announced that we believe that the optimal drug dose for the upcoming study is CF102 25.0 mg. This does was found to be the most effective dose out of the three dosages tested (1.0 mg, 5.0 mg and 25.0 mg) in the previous Phase I/II study. We filed a patent application protecting such optimal dose of CF102 for HCC. A publication summarizing the results of the Phase I/II study was published in "The Oncologist", a leading oncology scientific journal. We also highlighted that one patient has been treated with CF102 for over five years. Also as part of the Phase II study, we plan to examine the viral load of HCC patients who are also infected with HCV. If we observe a decrease in the viral load in the HCV sub-population during this forthcoming study, we intend to commence a separate Phase II study for the HCV indication.

The Phase II study is a randomized, double-blind, placebo controlled trial to be conducted in the U.S., Europe and Israel with an estimated 78 patients to be enrolled. CF 102 is being evaluated for efficacy and safety as a second-line treatment for advanced HCC in subjects with Child-Pugh B who failed Nexavar as a first line treatment. The primary endpoint of the study is overall patient survival. In March 2014, the study protocolwas approved by the Institutional Review Board at the Rabin Medical Center in Israel and in December 2014 we dosed the first patient at the study's Israeli site.

Additional Developments with CF102

JC Virus

In April 2011, we announced that, in laboratory study, CF102 inhibited the reproduction of the JC virus, a type of polyomavirus, which is dormant in approximately 70% to 90% of the world population. However, in patients treated with biological drugs, including monoclonal antibody therapeutics, such as anti-TNFs or anti-CD20, JC virus replication may occur, resulting in development of progressive multifocal leukoencephalopathy, or PML, which is characterized by progressive damage or inflammation of the white matter of the brain and, eventually, death. The ability of CF102 to suppress the JC Virus culture, as indicated in the laboratory study, may indicate that it may be used for the treatment of PML as a combination therapy with biological drugs. As CF102 is already in various stages of clinical development for other indications, its efficacy for this new application may be tested in clinical trials.

CF602

The allosteric modulator, CF602, is our third drug candidate in its pipeline. CF602 is an orally bioavailable small molecule, which enhances the affinity of the natural ligand, adenosine, to its A3AR. The advantage of this molecule is its capability to target specific areas where adenosine levels are increased. Normal body cells and tissues are refractory to allosteric modulators. This approach complements the basic platform technology of Can-Fite, utilizing the Gi coupled protein A3AR as a potent target in inflammatory diseases. CF602 has demonstrated proof of concept for anti-inflammatory activity in *in vitro* and *in vivo* studies performed by us.

Recently, CF602 was tested in an experimental animal model of diabetic rats, which similar to diabetic patients, suffer from sexual dysfunction. Erectile dysfunction was assessed by monitoring the ratio between intra-cavernosal pressure (ICP) and mean arterial pressure (MAP) as a physiological index of erectile function. The ICP/MAP for the CF602 treated group improved by 118% over the placebo group. This data is similar to that achieved earlier by sildenafil (Viagra) in preclinical studies. In addition, treatment with CF602 reversed smooth muscle and endothelial damage, in a dose dependent manner, leading to the improvement in erectile dysfunction. Subject to having sufficient financial resources, we intend to conduct further pre-clinical studies for this drug candidate. After completion of all pre-clinical testing, we intend to file an IND with respect to CF602.

During clinical studies conducted with our product candidates, other than CF602, patients suffering from sexual dysfunction reported that they returned to normal functioning following the treatment with such drugs. We believe that these findings are correlated with our platform technology, which is the targeting of the A3AR. Adenosine, like nitric oxide, is a potent and short-lived vaso-relaxant that functions via intracellular signaling (in particular, through cAMP) to promote smooth muscle relaxation. Recent studies conducted by others show that adenosine functions to relax the corpus cavernosum and thereby promote penile erection. We have filed a patent application in Israel for the treatment of sexual dysfunction utilizing our drug candidates and are planning to develop CF602 for this indication as it uses the same platform technology and becomes active through the same mechanism as the rest of our drug candidates. GlobalData valued the erectile dysfunction therapeutic market at $2.9 billion in 2010 reducing to $2.6 billion by 2018, which mainly includes the drugs Viagra, Cialis and Levitra.

Commercial Biomarker Test

In March 2015, we completed the development of a commercial predictive biomarker blood test kit for A3AR. The biomarker test can be used at any molecular biology lab, where a small blood sample from a prospective patient would be tested and within just a few hours, results indicate if the patient would benefit from treatment with our drugs, which are currently in clinical trials for rheumatoid arthritis, psoriasis, and liver cancer.

The U.S. Patent and Trademark Office previously issued to us a patent for the utilization of A3AR as a biomarker to predict patient response to its drug CF101 in autoimmune inflammatory indications.

In-Licensing Agreements

The following are summary descriptions of certain in-licensing agreements to which we are a party. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this Annual Report on Form 20-F.

NIH Agreement

On January 29, 2003, we entered into a license agreement with the NIH, or the NIH Agreement, through the U.S. Public Health Service. Pursuant to the NIH Agreement, we were granted an exclusive license for the use of a family of U.S. and European patents and patent applications relating to CF101, CF102 and other small molecules and for the use, sale, production and distribution of products derived from such patents around the world. Subject to certain conditions, we may sublicense the NIH Agreement. However, the NIH retains a paid-up, worldwide license to practice the licensed inventions for government purposes and may require us to grant sublicenses when necessary to fulfill health or safety needs.

According to the NIH Agreement, we are committed to pay royalties as follows: (i) a $225,000 signing payment; (ii) a minimum non-refundable annual payment of $50,000; (iii) 4% to 5.5% of our total net revenues from sales of licensed products or from conducting tests with respect to CF101, CF102 and the other licensed small molecules worldwide, on a consolidated basis, out of which 1.75%-2.75% may be offset against royalties that we are required to pay another third party; (iv) individual payments ranging from $25,000 to $500,000 subject to meeting certain drug development milestones, including the initiation of certain clinical trials with respect to the licensed products; and (v) additional payments totaling 20% of all monetary consideration received from sublicensees, except for royalties received on any such sublicensee's net revenues from sales of the licensed products, out of which 2% may be offset against royalties that we are required to pay another third party. As of December 31, 2014, we have paid approximately $1,025,000 in royalties to the NIH in connection with the NIH Agreement. We estimate that we will further pay a total of approximately $425,000 in milestone payments to the NIH in connection with the NIH Agreement until its expiration.

The NIH Agreement sets certain development milestones with which we must comply. On August 4, 2005 and February 4, 2013, amendments were signed with the NIH to extend such milestone dates. The amendments had no effect on the originally determined license terms.

The NIH Agreement will remain in effect until the last patent licensed under the NIH Agreement expires on June 30, 2015, unless it is earlier terminated by one of the parties, according to the NIH Agreement. The termination rights include, but are not limited, our right to terminate upon 60-days' prior written notice to the NIH, the NIH's right to terminate if we become insolvent or bankruptcy proceedings are initiated against us, and NIH's right to terminate upon our default in the performance of any material obligation and our failure to cure such default within 90 days of written notice of such default.

In addition, on January 24, 2006, we entered into a cooperative research and development agreement, or CRADA, with the NIH whereby we received an option to obtain a license from the NIH for any new group of A3AR agonists to be developed under terms that will be determined between the parties on the date of exercise of such option. In connection with the CRADA and the option granted thereunder, we signed a commercial evaluation license agreement with the NIH on April 17, 2007, and selected one molecule, CF502 (or MRS3558) to evaluate. However, at a later stage, we decided not to continue the development of CF502, terminated the commercial evaluation license agreement and did not exercise the option granted under the CRADA.

Leiden University Agreements

On November 2, 2009, we entered into a license agreement, or the Leiden University Agreement, with Leiden University. Leiden University is affiliated with the NIH and is the joint owner with the NIH of the patents licensed pursuant to the Leiden University Agreement. The Leiden University Agreement grants an exclusive license for the use of the patents of several compounds, including CF602, that comprise certain allosteric compound drugs, and for the use, sale, production and distribution of products derived from such patents in the territory, i.e., China and certain countries in Europe (Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland, Holland and England). Subject to certain conditions, we may sublicense the Leiden University Agreement. However, the U.S. government has an irrevocable, royalty-free, paid-up right to practice the patent rights throughout the territory on behalf of itself or any foreign government or international organization pursuant to any existing or future treaty or agreement to which the U.S. government is a signatory and the U.S. government may require us to grant sublicenses when necessary to fulfill health or safety needs.

Pursuant to the Leiden University Agreement, we are committed to make the following payments: (i) a one-time concession commission of 25,000 Euros; (ii) annual royalties of 10,000 Euros until clinical trials commence; (iii) 2% to 3% of net sales value, as defined in the Leiden University Agreement, received by us; (iv) royalties of up to 850,000 Euros based on certain progress milestones in the clinical stages of the products which are the subject of the patent under the Leiden University Agreement; and (v) if we sublicense the agreement, we will provide Leiden University royalties at a rate of 2-3% of net sales value, as defined in the Leiden University Agreement, and 10% of certain consideration received for granting the sublicense. In the event that we transfer to a transferee the aspect of our business involving the Leiden University Agreement, we must pay to Leiden University an assignment royalty of 10% of the consideration received for the transfer of the agreement. However, a merger, consolidation or any other change in ownership will not be viewed as an assignment of the agreement. In addition, we have agreed to bear all costs associated with the prosecution of the patents and patent applications to which we are granted a license under the Leiden University Agreement. As of December 31, 2014, we have paid approximately 85,000 Euros in royalties to Leiden University in connection with the Leiden University Agreement.

The Leiden University Agreement expires when the last of the patents expires in each country of the territory, unless earlier terminated in accordance with the terms of the Leiden University Agreement. The last of such patents is set to expire on 2027. The termination rights of the parties include, but are not limited to, (i) the non-defaulting party's right to terminate if the defaulting party does not cure within 90 days of written notice identifying the default and requesting remedy of the same; and (ii) Leiden University's right to terminate if we become insolvent, have a receiver appointed over our assets or initiate a winding-up. In addition, Leiden University may terminate the agreement when it is determined, in consultation with NIH, that termination is necessary to alleviate health and safety needs and certain other similar circumstances.

Out-Licensing and Distribution Agreements

The following are summary descriptions of certain out-licensing and distribution agreements to which we are a party. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this Annual Report on Form 20-F.

Seikagaku Agreement

On September 22, 2006, we executed an exclusive license agreement, which was amended in December 2006, with Seikagaku Corporation, a Japanese public corporation, or SKK, for the use, development and marketing of CF101 in Japan with respect to inflammatory indicators, except for ophthalmic disease indicators. The agreement with SKK as amended, or the Seikagaku Agreement, also grants to SKK an exclusive, royalty-free license to use certain of our trademarks, as determined from time to time, in connection with the distribution, marketing, promotion and sale of any products derived from CF101 pursuant to the Seikagaku Agreement. Under the terms of the Seikagaku Agreement, we cannot prevent SKK from making financial, operational or strategic decisions associated with the use, development or marketing of CF101 in Japan.

The Seikagaku Agreement contemplates the creation of a four member joint committee consisting of two members from each party with the purpose of serving as a joint source of experience and knowledge in CF101 development and to facilitate communication and coordination between the parties with respect to such development. The joint committee, among other things specifically identified in the Seikagaku Agreement, provides to the parties opinions, proposals, ideas and updates with respect to the CF101 development processes conducted separately by each party.

Under the Seikagaku Agreement, we are entitled to up-front and milestone payments of up to $17 million (of which $2 million is attributable to our participation in certain research and development activities), annual payments of $500,000 and at least an additional $1 million in milestone payments if SKK pursues a second indication (the current indication is RA).We will also be entitled to royalties in an amount between 7-12% of annual net sales in Japan subject to certain sales criteria. In accordance with the Seikagaku Agreement, we received an up-front payment of $3.0 million in 2006, a milestone payment of $1.0 million in 2008 and $0.5 million per year from 2007 through 2011 as an annual minimum royalty payment (for an aggregate of $2.5 million). In addition to the amounts above, we will be entitled to additional payments based on sales of raw materials to SKK for the purpose of developing, producing and marketing CF101. If SKK decides to produce the raw materials itself, we will be entitled to $1.0 million and an additional manufacturing royalty payment. Furthermore, we will be entitled to receive additional payments if SKK requests information regarding the results and reports of other clinical and non-clinical studies conducted by us and we will be required to make certain payments to SKK if we request results and reports from their clinical and non-clinical studies. These payments will be calculated based on a percentage of the costs of such clinical and non-clinical studies, as the case may be.

Pursuant to a representative agreement, dated September 22, 2006, we have paid or are committed to pay, 5% of the above amounts actually received as a brokerage commission to Fuji Techno Interface Ltd., the Japanese company that brokered the Seikagaku Agreement. The Seikagaku Agreement is effective until SKK completes all payments required by the agreement, unless it is earlier terminated as a result of a material breach not cured within the specified time frame or as a result of the initiation of bankruptcy or insolvency- related proceedings.

As of December 31, 2014, SKK had paid us approximately $8.5million in up-front and milestone payments.

Kwang Dong Agreements

On December 22, 2008, we entered into a license agreement with Kwang Dong Pharmaceutical Co. Ltd, a South Korean limited company, or KD, and the Kwang Dong License Agreement, respectively, for the use, development and marketing of CF101 in the Republic of Korea with respect to RA. In addition, the Kwang Dong License Agreement grants to KD an exclusive, royalty-free license to use certain of our trademarks, as determined from time to time, in connection with the distribution, marketing, promotion and sale of any products derived from CF101 pursuant to the Kwang Dong License Agreement.

The Kwang Dong License Agreement also provides for the creation of a four member joint committee consisting of two members from each party for the purpose of serving as a joint source of experience and knowledge in CF101 development and to facilitate communication and coordination between the parties with respect to such development. The joint committee will, among other things specifically identified in the Kwang Dong License Agreement, provide to the parties opinions, proposals, ideas and updates with respect to the CF101 development processes conducted separately by each party.

According to the Kwang Dong License Agreement, we are entitled to receive or have received the following payments: (i) a non-refundable amount of $300,000 paid within 30 days of the effective date of the agreement; (ii) an amount of up to $1.2 million based on our compliance with certain milestones, including but not limited to, the conclusion of the Phase II clinical trial for CF101 for treating RA and the receipt of various regulatory authorizations; and (iii) annual royalties of 7% of annual net sales of the licensed drug in the Republic of Korea. In addition to the amounts detailed above, we will be entitled to additional payments based on sales of raw materials to KD for the purpose of developing, producing and marketing CF101.

The Kwang Dong License Agreement is effective until KD completes all payments required thereunder, unless it is earlier terminated as a result of a material breach not cured within the specified time frame, the breach by KD of the Kwang Dong Purchase Agreement or the initiation of bankruptcy or insolvency related proceedings.

Pursuant to a share purchase agreement entered into with KD at the same time as the Kwang Dong License Agreement, KD purchased 95,304 of our ordinary shares, representing approximately 1.0 % of our share capital on a fully diluted basis, as of the date of the purchase. The shares were purchased for a premium of 50% on the shares' average closing price for the ten days preceding December 11, 2008, or a purchase price of NIS 0.455 per share.

After the TASE approved such shares for the listing for trade on January 5, 2009, the shares were allocated to KD and the transaction was finalized in January 2009.As of December 31, 2014, KD had paid us approximately $0.8million, which represents milestone payments pursuant to the Kwang Dong License Agreement, an advance of certain amounts to become due under the Kwang Dong License Agreement and the purchase price for the shares.

Cipher Pharmaceuticals Agreement

On March 20, 2015, we entered into a Distribution and Supply Agreement with Cipher Pharmaceuticals, or Cipher, granting Cipher the exclusive right to distribute CF101 in Canada for the treatment of psoriasis and RA.

Under the Distribution and Supply Agreement, we are entitled to CDN$1.65 million upon execution of the agreement plus milestone payments upon receipt of regulatory approval by Health Canada for CF101 and the first delivery of commercial launch quantities as follows (i) CDN$1 million upon the first approved indication for either psoriasis or RA, and (ii) CDN $1 million upon the second approved indication for either psoriasis or RA. In addition, following regulatory approval, we shall be entitled to a royalty of 16.5% of net sales of CF101 in Canada and reimbursement for the cost of manufacturing CF101. We are also entitled to a royalty payment for any authorized generic of CF101 that Cipher distributes in Canada.

We are responsible for supplying Cipher with finished product for distribution and conducting product development activities while Cipher is responsible for distribution, marketing and obtaining applicable regulatory approvals in Canada. The Distribution and Supply Agreement has an initial term of fifteen years, automatically renewable for additional five year periods and may be terminated in certain limited circumstances including certain breaches of the agreement and failure to achieve certain minimum quantities of sales during the contract period.

The timeline to regulatory submissions to Health Canada will be determined by the completion of the remaining clinical trial program.

Eye-Fite Agreement

In connection with the spin-off transaction described below in "Item 10. Additional Information—Material Contracts—OphthaliX Agreements", on November 21, 2011, we entered into a license agreement, or the Eye-Fite Agreement, with Eye-Fite according to which we (i) granted Eye-Fite a sole and exclusive worldwide license for the use of CF101 solely in the field of ophthalmic diseases and patent rights which we received under the NIH Agreement, with respect to CF101 in the field of ophthalmic diseases for research, development, commercialization and marketing throughout the world and (ii) assigned to Eye-Fite our rights, title and interest in and to any and all INDs to CF101 in the ophthalmic field. As consideration for the grant of the license, we received 999 ordinary shares of Eye-Fite, in addition to the one share we already had, which resulted in us owning all of the issued and outstanding shares of Eye-Fite, all of which were transferred to OphthaliX in connection with this transaction. In addition, Eye-Fite must, for the duration of the NIH Agreement, make the following payments to the NIH: (i) a nonrefundable minimum annual royalty of $25,000, (ii) earned royalties of 4.0% to 5.5% on net sales in territories in where such patents exist and (iii) individual payments ranging from $25,000 to $500,000 upon the achievement of various development milestones for each indication. Eye-Fite will also be required to make payments to the NIH of 20% of sublicensing revenues, excluding royalties and net of the required milestone payments. The payments set forth above represent our liabilities to the NIH under to the NIH Agreement, which pursuant to the Eye-FiteAgreement, Eye-Fite is obligated to make to the NIH.

If Eye-Fite fails to make a required payment to the NIH, Can-Fite will be entitled to terminate the license granted to Eye-Fite under the Eye-Fite Agreement upon 30 days' prior written notice. The Eye-Fite Agreement will remain in effect until the expiration of the last of the patents licensed thereunder, unless earlier terminated by one of the parties in accordance with its terms. Can-Fite may terminate the Eye-Fite Agreement upon customary bankruptcy and insolvency events of Eye-Fite and upon Eye-Fite's material breach of the Eye-Fite Agreement, upon 30 days' prior written notice. Eye-Fite may terminate the Eye-Fite Agreement upon three months' prior written notice for any reason and upon 30 days' prior written notice for Can-Fite's material breach of the Eye-Fite Agreement. All inventions resulting from the development and commercialization of CF101 under the Eye-Fite Agreement belong to Can-Fite, whether invented solely by Can-Fite, solely by Eye-Fite or by both entities. However, the Eye-Fite Agreement also grants Eye-Fite an exclusive license to use any such inventions in the field of ophthalmic diseases around the world for no additional consideration.

Total Revenues by Category of Activity and Geographic Markets

We have not generated any revenues during the prior three fiscal years. Historically, we have generated revenues from payments received pursuant to our out-licensing agreements with SKK and KD with respect to CF101.See "Item 4—Information on the Company—Business Overview—Out-Licensing and Distribution Agreements". We expect to generate future revenues through our current and potential future out-licensing arrangements with respect to CF101, as well as through future out-licensing arrangements with respect to our other product candidates, i.e., CF102 and CF602.

Seasonality

Our business and operations are generally not affected by seasonal fluctuations or factors.

Raw Materials and Suppliers

We believe that the raw materials that we require to manufacture CF101, CF102 and CF602 are widely available from numerous suppliers and are generally considered to be generic industrial chemical supplies. We do not rely on a single or unique supplier for the current production of any therapeutic small molecule in our pipeline.

Manufacturing

We are currently manufacturing our active pharmaceutical ingredient, or API, through a leading Chinese contract research organization, or CRO. The relevant suppliers of our drug products are compliant with both current Good Manufacturing Practices, or cGMP, and current Good Laboratory Practices, or cGLP, and allow us to manufacture drug products for our current clinical trials. We anticipate that we will continue to rely on third parties to produce our drug products for clinical trials and commercialization.

There can be no assurance that our drug candidates, if approved, can be manufactured in sufficient commercial quantities, in compliance with regulatory requirements and at an acceptable cost. We and our contract manufacturers are, and will be, subject to extensive governmental regulation in connection with the manufacture of any pharmaceutical products or medical devices. We and our contract manufacturers must ensure that all of the processes, methods and equipment are compliant with cGMP for drugs on an ongoing basis, as mandated by the FDA and other regulatory authorities, and conduct extensive audits of vendors, contract laboratories and suppliers.

Contract Research Organizations

We outsource certain preclinical and clinical development activities to CROs, which in pre-clinical studies work according to cGMP and cGLP. We believe our clinical CROs comply with guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, which attempt to harmonize the FDA and the European Medicines Agency, or the EMA, regulations and guidelines. We create and implement the drug development plans and, during the preclinical and clinical phases of development, manage the CROs according to the specific requirements of the drug candidate under development.

Marketing and Sales

We do not currently have any marketing or sales capabilities. We intend to license to, or enter into strategic alliances with, larger companies in the pharmaceutical business, which are equipped to market and/or sell our products, if any, through their well-developed marketing capabilities and distribution networks. We intend to out-license some or all of our worldwide patent rights to more than one party to achieve the fullest development, marketing and distribution of any products we develop.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that we believe are important to the development of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary position.

Patents

As of March 23, 2015, we owned or exclusively licensed (from the NIH and Leiden University) 15 patent families that, collectively, contain approximately 150 issued patents and pending patent applications in various countries around the world relating to our two clinical candidates, CF101 and CF102, and our preclinical candidate, CF602. Patents related to our drug candidates may provide future competitive advantages by providing exclusivity related to the composition of matter, formulation and method of administration of the applicable compounds and could materially improve their value. The patent positions for our leading drug candidates are described below.

We currently license from the NIH and Leiden University certain intellectual property that is necessary to conduct our business. We currently hold an exclusive license from the NIH to a family of patents that protects certain small molecules that are A3AR agonists, such as CF101 and CF102, and the pharmaceutical use of such molecules. This exclusive license relates to two compositions of matter patents that were granted in the United States and Europe (in particular, United Kingdom, France, Germany, Switzerland, Italy, Belgium and Luxembourg), the former of which is expected to expire in 2015 and the latter in 2014. We will not be able to extend the foregoing expiration dates and as such, as of June 30, 2015, the license agreement with the NIH will terminate. We do not expect that we will be able to submit an NDA seeking approval of CF101 or CF102 prior to the composition of matter patents' respective expiration dates. However, because CF101 and CF102 each may be a new chemical entity, or NCE, following approval of an NDA, we, if we are the first applicant to obtain NDA approval, may be entitled to five years of data exclusivity in the United States with respect to such NCEs. Analogous data and market exclusivity provisions, of varying duration, may be available in Europe and other foreign jurisdictions. We also have rights under our pharmaceutical use issued patents with respect to CF101 and CF102, which provide patent exclusivity within our field of activity until the mid- to late-2020s. While we believe that we may be able to protect our exclusivity in its field of activity through such use patent portfolio and such period of exclusivity, the lack of composition of matter patent protection may diminish our ability to maintain a proprietary position for its intended uses of CF101 and CF102. Moreover, we cannot be certain that we will be the first applicant to obtain an FDA approval for any indication of CF101 and we cannot be certain that we will be entitled to NCE exclusivity. Such diminution of our proprietary position could have a material adverse effect on our business, results of operation and financial condition. We also currently hold an exclusive license from the NIH and Leiden University of the Netherlands to a family of patents and patent applications that relate to the allosteric modulators of the A3AR, which includes the allosteric modulator CF602. This exclusive license relates to two patents that were granted in the United States, China and in Europe (validated in, Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland, Holland and England). These granted patents and the patents that may be granted on patent applications of this patent family are set to expire in 2027. We hold the foregoing licenses pursuant to the terms and conditions of certain license agreements.

With respect to our product candidates, we currently own patents and/or have patent applications pending in several countries around the world for the following families of patents:

- a family of patents which pertains to the use of substances that bind to the A3AR, including CF101 and CF102; the pharmaceutical uses to which such family relates include the treatment of proliferative diseases, such as cancer, psoriasis and autoimmune diseases. Such patents were granted in the United States, Europe (by the European Patent Office, or the EPO, and validated in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Portugal, Spain, Sweden, Switzerland, Holland and the United Kingdom), Australia, Canada, Israel, China, Japan, South Korea, Mexico, Poland, Russia and Hong-Kong. These patents are set to expire in 2020, other than the United States patent that will expire in 2022;

- a family of patents and a patent application which pertain to use of substances that bind to the A3AR for the treatment of viral diseases, such as AIDS and hepatitis, and which inhibit viral replication. Such patents were granted in the United States, in Europe (by the EPO and validated in France, Germany, Italy, Switzerland and the United Kingdom), Australia, China, Israel, Japan, Singapore, Canada and Hong Kong. The patents are set to expire in 2022, other than the United States patent that will expire in 2023. The patent application is pending in Brazil with a filing date of January 1, 2002 and a priority date of January 16, 2001;

- a patent which pertains to the use of A3AR agonists for the treatment of inflammatory arthritis, in particular RA. This patent was granted in the United States and is set to expire in 2023;

- a family of patents and patent applications which pertain to a method of identifying inflammation, determining its severity, and determining and monitoring the efficacy of the anti-inflammatory treatment by determining the level of A3AR expression in white blood cells as a biological marker for inflammation. These patents were granted in certain countries in Europe (by the EPO and validated in France, Germany, Italy, Spain, Switzerland and the United Kingdom), Australia, Israel, Japan, USA, China and Mexico. The patents are set to expire in 2025. The patent applications are pending in the Canada, and Brazil. Each of the applications has a filing date of November 30, 2005 and a priority date of December 2, 2004;

- a family of patents and patent applications which pertain to the use of A3AR agonists for the treatment of DES. This family includes patents in Japan and Mexico. These patents are set to expire in 2026.

- a family of patents and patent applications which pertains to the use of A3AR agonists for the treatment of reducing IOP. Such patents were granted in Australia and United States. The patents are set to expire in 2030. The patent applications are pending in the EPO (this European application designates all EPC member states), Israel, Japan, China, Canada, Mexico and South Korea, each with a filing date of May 16, 2010 and a priority date of May 17, 2009;

- a family of patents and patent applications which pertains to the use of a specific dose level of CF101 (total daily dose of 4.0 mg) for the treatment of psoriasis. Such a patent was granted in the United States. The patent is set to expire in 2030.The patent applications are pending in the China, the EPO (this European application designates all EPC member states), Israel (which was recently allowed) India, Japan and South Korea, each with a filing date of September 6, 2010 and a priority date of September 6, 2009;

- a family of patents and patent applications which pertain to the method for producing CF101. Such patents were granted in China, Japan and Israel. These patents are set to expire in 2028. The patent applications are pending in the United States, the EPO (this European application designates all EPC member states) and India, each with a filing date of March 13, 2008 and a priority date of March 14, 2007;

- a family of patents and patent applications which pertain to the use of A3AR agonists for the treatment of OA. Such patents were granted in Europe (by the EPO and validated in Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland, Holland and the United Kingdom), Australia, Canada, South Korea, China and Mexico. The patents are set to expire in 2026. Patent applications are pending in the United States, Brazil, Israel and Japan. These patent applications have a filing date of November 29, 2006 and a priority date of November 30, 2005;

- a family of patents and patent applications which pertains to the use of A3AR agonists for increasing liver cell division, intended to induce liver regeneration following injury or surgery. Such patents were granted in China, Israel, Japan, USA and Europe (by the EPOand validated in Austria, Belgium, Denmark, France, Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland and Turkey). There is one patent application pending in the United States with a filing date of October 22, 2007 and a priority date of October 15, 2007.

- a family of patent applications which pertain to the use of A3AR agonists for the maintenance of liver function in patients having chronic liver disease. These patent applications are pending in China, Israel, Japan, Hong-Kong, United States and Europe (this European application designates all EPC member states). These patent applications have a filing date of August 8, 2013 and a priority date of January 23, 2012;

- a family of patent application under joint ownership with the NIH and licensed, to the extent of our ownership, to Eye-Fite, which pertain to the use of A3AR agonists for the treatment of uveitis. These patent applications are pending in the Canada, Israel, Mexico and South Korea. The patent applications have filing dates of February 27, 2011 and priority dates of March 3, 2010;

- a patent application which pertains to the treatment of hepatocellular carcinoma. This patent application is a PCT application with a filing date of January 23, 2013 and a priority date of January 23, 2012;

- a family of patent applications which pertain to treatment of sexual dysfunction. This family includes patent applications in Israel (two), Australia, China, Japan, Russia, Brazil, Canada, Europe, India, Mexico, South Korea, and USA. The two Israeli patent applications have filing dates of August 8, 2012 and November 12, 2012 and the other patent applications have a filing date of August 8, 2013 with priority dates of August 8, 2012 and November 12, 2012.

We believe that our owned and licensed patents provide broad and comprehensive coverage of our technology, and we intend to aggressively enforce our intellectual property rights if necessary to preserve such rights and to gain the benefit of our investment. However, the patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, circumvented or found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. Neither we nor our licensors can be certain that we were the first to invent the inventions claimed in our owned or licensed patents or patent applications. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us, and the rights granted under any issued patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

Trade Secrets

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and assignment of inventions agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, such agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors or others.

Scientific Advisory Board

We seek advice from our Scientific Advisory Board on scientific and medical matters generally. We call for Scientific Advisory Board meetings on an as-needed basis. The following table sets forth certain information with respect to our Scientific Advisory Board members.

Name	Position/Institutional Affiliation
Nabil Hanna, Ph.D.	Former Chief Science Officer of Biogen-Idec
Kamel Khalili, Ph.D.	Temple University, Philadelphia, Pennsylvania

Clinical Advisory Board

Our Clinical Advisory Board, which consists of three members, a leading U.S.-based rheumatologist, oncologist and dermatologist, plays an active role in consulting with us with respect to clinical drug development. We call for Clinical Advisory Board meetings on an as-needed basis. The following table sets forth certain information with respect to our Clinical Advisory Board members.

Name	Position/Institutional Affiliation
Dr. Michael Weinblatt	Head, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital
Dr. Keith Stuart	Chairman, Department of Hematology and Oncology; Professor of Medicine, Tufts University School of Medicine; Lahey Clinic Medical Center
Dr. Jonathan Wilkin	Former Head, Dermatology Division, FDA

Competition

The pharmaceutical industry is characterized by rapidly evolving technology, intense competition and a highly risky, costly and lengthy research and development process. Adequate protection of intellectual property, successful product development, adequate funding and retention of skilled, experienced and professional personnel are among the many factors critical to success in the pharmaceutical industry.

Our technology platform is based on the finding that the A3AR is highly expressed in pathological cells, such as various tumor cell types and inflammatory cells. We believe that targeting the A3AR with synthetic and highly selective A3AR agonists, such as CF101 and CF102, and allosteric modulators, such as CF602, induces anti-cancer and anti-inflammatory effects. Currently, our drug candidates, CF101, CF102 and CF602 are being developed to treat several autoimmune-inflammatory, oncological and ophthalmic indications, including but not limited to: psoriasis; RA; OA; DES; glaucoma; uveitis; HCC and HCV. Preclinical studies have also indicated that our drug candidates have the potential to treat additional inflammatory diseases, such as Crohn's disease, oncological diseases and viral disease, such as the JC virus.

Despite the competition, however, we believe that our drug candidates have unique characteristics and advantages over certain drugs currently available on the market and under development to treat these indications. We believe that our pipeline of drug candidates has exhibited a potential for therapeutic success with respect to the treatment of autoimmune-inflammatory, oncological and ophthalmic diseases. We believe that targeting the A3AR with synthetic and highly selective A3AR agonists, such as CF101 and CF102, and allosteric modulators, such as CF602, induces anti-cancer and anti-inflammatory effects.

We believe the characteristics of CF101, as exhibited in our clinical studies to date, including its good safety profile, clinical activity, simple and less frequent delivery through oral administration and its low cost of production, position it well against the competition in the autoimmune-inflammatory markets, including the psoriasis and RA markets, where treatments, when available, often include injectable drugs, many of which can be highly toxic, expensive and not always effective. Moreover, pre-clinical pharmacology studies in different experimental animal models of arthritis revealed that CF101 acts as a disease modifying anti-rheumatic drug, or a DMARD, which, when coupled with its good safety profile, make it competitive in the psoriasis, RA and OA markets. Our recent findings also demonstrate that a biological predictive marker can be utilized prior to treatment with CF101, which may allow it to be used as a personalized medicine therapeutic approach for the treatment of RA. We believe CF101 is also well-positioned against some of the competition in the ophthalmic markets, where treatments, when available, often include frequent self-administered eye drops, which may be more difficult than taking pills and may result in less than the full dose of the drug actually entering the eye, have undesirable side effects and do not simultaneously treat the underlying cause and relieve the symptoms associated with the indication. Like CF101, CF102 has a good safety profile, is orally administered and has a low cost of production, which we believe positions it well in the HCC market, where only one drug, Nexavar, has been approved by the FDA.

In addition, our human clinical data suggests that A3AR may be a biological marker in that high A3AR expression prior to treatment has been predictive of good patient response to our drug treatment. In fact, as a result of our research we have developed a simple blood assay to test for A3AR expression as a predictive biological marker. We have applied for a patent with respect to the intellectual property related to such assay and are currently utilizing this assay in our ongoing Phase IIb study of CF101 for the treatment of RA.

On the other hand, other drugs on the market, new drugs under development (including drugs that are in more advanced stages of development in comparison to our drug pipeline) and additional drugs that were originally intended for other purposes, but were found effective for purposes targeted by us, may all be competitive to the current drug candidates in our pipeline. In fact, some of these drugs are well established and accepted among patients and physicians in their respective markets, are orally bioavailable, can be efficiently produced and marketed, and are relatively safe. Moreover, other companies of various sizes engage in activities similar to ours. Most, if not all, of our competitors have substantially greater financial and other resources available to them. Competitors include companies with marketed products and/or an advanced research and development pipeline. The major competitors in the arthritis and psoriasis therapeutic field include Abbott Laboratories, Johnson & Johnson, Amgen, Roche, Pfizer, Novartis, Astellas, Eli Lilly and more. The competitive landscape in the ophthalmic therapeutics field includes Novartis/Alcon, Allergan, Pfizer, Roche/Genentech, Merck (which acquired Inspire Pharmaceuticals), Santen (which acquired Novagali), Bausch & Lomb (which acquired ISTA Pharmaceuticals and is currently being acquired by Valeant), GlaxoSmithKline, or GSK, Sanofi-Aventis (which acquired Fovea) and more. Competitors in the HCC field include companies such as Onyx, Bayer, Bristol-Myers Squibb, Abbott Laboratories, Eli Lilly, Arqule and more. Competitors in the HCV field include companies such as Merck, Vertex, Roche, Bristol-Myers Squibb (which acquired Inhibitex), Gilead Sciences (which acquired Pharmasset), Achillion, Idenix, Valeant, Human Genome Sciences, Abbott, AstraZeneca, BoehringerIngelheim, Novartis, Pfizer, Idenix, Johnson & Johnson, Presidio, Medivir, Celgene, Enanta, GSK and more.

Moreover, several companies have reported the commencement of research projects related to the A3AR. Such companies include CV Therapeutics Inc. (which was acquired by Gilead), King Pharmaceuticals R&D Inv. (which was acquired by Merck), Hoechst Marion Roussel Inc., Novo Nordisk A/S and Inotek Pharmaceuticals. However, we are not aware if such projects are ongoing or have been completed and, to the best of our knowledge, there is no approved drug currently on the market which is similar to our A3AR agonists, nor are we aware of any allosteric modulatorin the A3AR product pipeline similar to our allosteric modulator with respect to chemical profile and mechanism of action.

CF101 for the Treatment of Psoriasis

Psoriasis is a skin condition that affects 2% to 3% of the general population according to the National Psoriasis Foundation. The disease is manifested by scaly plaques on the skin and in the severe form has a major effect on the physical and emotional well-being of the patients. Topical agents are typically used for mild disease, phototherapy for moderate disease, and systemic agents for severe disease. For moderate to severe cases, systemic biologic drugs, delivered via IV, have dominated the market. According to the National Psoriasis Foundation, common side effects of biologics include respiratory infections, flu-like symptoms, and injection site reactions while rare side effects include serious nervous system disorders, such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes, blood disorders, and certain types of cancer. We believe a significant need remains for novel oral and safe drugs for patients who do not respond to existing therapies or for whom these therapies are unsuitable.

The psoriasis therapeutic market is dominated by biological drugs that are primarily administered via intravenous injection (IV) and have potential side effects. According to Global Data, the psoriasis treatment market was worth $3.6 billion in 2010 and is forecast to grow to $6.7 billion by 2018.

The current common treatments for psoriasis include topical and systemic drugs, steroids, immunosuppressive drugs such as Cyclosporine A by Novartis, MTX and biological drugs. Biological drugs, such as Enbrel by Amgen and Pfizer, Amevive by Astellas and Ustakinumab by Centocor, a division of Johnson & Johnson, have significant side effects, are expensive and patients are often not responsive. Many of the current RA drugs on the market or in development are also used for the treatment of psoriasis. See “—CF101 for the Treatment of RA.” In addition, several therapies are in advanced clinical development for psoriasis and many others are in Phase II or earlier stages of development.

CF101 for the Treatment of RA

RA is a severe disease that attacks approximately 0.6% of the U.S. population, mainly women and, in particular, postmenopausal women. According to Visiongain, the world RA market size is predicted to generate revenues of $38.5 billion in 2017.

Many drugs are used to treat RA, including DMARDs. These include MTX, plaquenil, sulfasalazine and leflunomide, all of which are small molecule drugs with mild effectiveness. MTX is the most commonly administered DMARD for RA. It is a generic chemotherapeutic agent marketed by several manufacturers that is administered orally. Due to its relatively toxic nature, however, MTX may result in severe side effects.

The second class of DMARD includes biological drugs, such as Enbrel by Amgen Inc. (which contains the active ingredient Etanercept), Remicade by Centocor, a division of Johnson & Johnson (which contains the active ingredient Infliximab) and Humira by Abbott Laboratories (which contains the active ingredient Adalimumab). These drugs are usually administered in combination with MTX and are more effective in combination, but may have severe side effects, including lymphoma. Biological drugs are administered through injection, are generally expensive and there is no biomarker to predict the response, if any. Steroidal drugs are also used to reduce the general activity of the immune system and for pain relief. In addition, the FDA recently approved Pfizer's Xeljanz (tofacitinib) small molecule drug, which is the first JAK inhibitor drug, or a drug that inhibits the effect of one or more of the enzymes in the janus kinase family, or a family enzymes that transfer cytokine-mediated signals, to treat RA. Moreover, several therapies, including biological drugs and small molecule drugs, are in advanced clinical development for RA, while others are in Phase II or earlier stages of development.

CF101 for the Treatment of OA

According to Transparency Market Research global osteoporosis market is estimated to be $7.3 billion in 2010 and expected to reach $11.4 billion in 2015. The medications most commonly used to treat OA are symptom-modifying drugs, primarily generics, such as non-steroidal, anti-inflammatory drugs and cyclooxygenase 2 inhibitors, or COX-2 inhibitors, which directly target the COX-2 enzyme involved with the etiology and pathogenesis of inflammation and pain. There are no disease-modifying OA drugs, or DMOADs, currently approved for OA and the late stage drug pipeline also lacks DMOADs, except Novartis' SMC021, which hasn't met its primary end points in a Phase III study.

Current and future competition includes drugs being developed to relieve pain associated with OA and for the treatment of OA. In addition to DMOADs, therapies in development for OA include stem cell therapy, COX-2 inhibitors, cathepsin S inhibitors, or synthetic inhibitors of the cathepsin S protein, opioid receptor agonists, or pain relievers that bind to certain nervous system receptors, anti-nerve growth factor inhibitors, or inhibitors of proteins that promote nerve growth, transient receptor potential vanilloid-1 antagonists, or a pain reliever that binds to certain proteins responsible for heat and pain sensations, COX inhibiting nitric oxide donors, or drugs that act as COX inhibitors while donating nitric oxide and thereby promoting an anti-inflammatory effect, phosphodiesterase inhibitors, or drugs that block certain enzymes thereby preventing the inactivation of certain intracellular messaging, and calcitonin receptor agonists, or drugs that bind to receptors related to functional activity.

CF101 had a significant anti-inflammatory effect in pre-clinical pharmacology studies for OA and is currently in preparation for a Phase II study.

CF101 for the Treatment of Crohn's Disease

According to Transparency Market Research, the osteoporosis market will reach $6.8 billion in 2015. According to Datamonitor, in 2009, 890,000 persons were estimated to have Crohn's disease in the seven major markets (the U.S., Japan, France, Germany, Italy, Spain and the U.K.) and more than half of such patients were estimated to reside in the United States.

Therapies in development for Crohn's disease include interleukin inhibitors, a drug that inhibits cell growth, enzyme inhibitors, stem cell therapy, integrin antagonists, or drugs that bind to certain receptors that are responsible for the regulation of cell cycle, shape and motility, tumor necrosis factor inhibitors, or drugs that inhibit the factor that promotes inflammatory responses, and immunomodulators, or drugs that regulate the immune system.

Although CF101 was effective in our pre-clinical and pharmacological studies relating to Crohn's disease, we currently do not have any planned clinical trials with respect to the use of CF101 for the treatment of Crohn's disease.

CF101 for the Treatment of Glaucoma

According to Datamonitor, as of 2010, seven million people in the seven major markets suffered from glaucoma. GlobalData estimated that the market for glaucoma drugs was $3.0 billion in 2010 and forecasts growth with a compound annual growth rate of 0.6% between 2010 and 2018. We expect that the number of people who suffer from glaucoma will increase as the population in each of the seven major markets ages.

The main drugs used to treat glaucoma include Xalatan®, Travatan® and Cosopt®. Xalatan® is recommended by the European Glaucoma Society and American Academy of Ophthalmologists as the first choice for the treatment of glaucoma. According to a Pfizer annual report, Xalatan®, which is marketed by Pfizer, is the leading drug used to treat glaucoma, and had global sales of approximately $0.6 billion in 2013 compared to $1.2 billion in 2011.Travatan® was first launched in the United States in 2001 and then Europe and the certain other markets in 2002. According to Evaluate Pharma, Travatan®, marketed by Alcon, experienced sales of approximately $600 million in 2010 and 2011.Travatan® is administered once each day, which ophthalmologists cite as a significant advantage over other drugs used to treat glaucoma. Cosopt® is the oldest combination therapy in the glaucoma market. Due to the expiration of patents covering Cosopt® in 2008, some ophthalmologists have begun to look to other brands or generic drugs in the treatment of glaucoma. Another leading company in this field is Allergan, which markets Lumigan®, Ganfort™, Alphagan®, and Combigan®, with over $1.0 billion in aggregate revenues in 2011. The glaucoma therapeutics market has witnessed major revenues depletion in the recent years due to a string of patent expirations, which started with the expiration of the Xalatan® patent.

Several therapies are in advanced clinical development for glaucoma. In addition, in 2012, the FDA approved tafluprost ophthalmic solution, Zioptan by Merck, the first preservative-free prostaglandin analog ophthalmic solution, or a solution derived from fatty acids, for the treatment of glaucoma.

While several anti-glaucoma drugs exist, the glaucoma therapeutics market has a high level of unmet need, which mainly arises from the lack of approved drugs targeting the disease's progression. Many therapies approved provide only symptomatic relief. The therapies which are available for the treatment of glaucoma have shown low to moderate efficacy and safety profiles. Accordingly, there is a significant need for drugs that reduce IOP. In addition, part of the pathogenesis of glaucoma is damage to the optic nerve, so drugs that, in addition to lowering IOP, have a neuroprotective effect, would also satisfy an unmet need. Based on its toxicological profile, we believe that CF101 has the potential to have fewer side effects than existing drugs for the treatment of glaucoma. At the same time, CF101 offers the potential to act as a neuroprotective agent that prevents the death of retinal cells, as well as the potential to lower IOP. We also believe that CF101 will offer less frequent administration than most existing therapies.

CF101 for the Treatment of Uveitis

According to Data Monitor, uveitis is estimated as the fifth or sixth leading cause of blindness in the United States. The incidence of uveitis worldwide varies from 14 to 52.4 per 100,000 people, while the overall prevalence around the world is reported as 0.73%. We estimate that there are approximately one million uveitis patients around the world. According to GlobalData, in 2010, the uveitis market was $0.32 billion and is estimated to reach $1.6 billion by 2017. The current treatments for uveitis include corticosteroids, anti-metabolites, T-cell inhibitors, alkylating agents and biological drugs, which often involve serious adverse side effects and lack of efficacy. Accordingly, we believe that a need exists for drugs used in the treatment of uveitis that are less toxic and more effective. There are currently several therapies in advance clinical development for anterior and posterior uveitis.

We believe that a need exists for drugs used for the treatment of uveitis that are less toxic and more effective than currently available therapies. Former pre-clinical pharmacology studies demonstrated that CF101 is effective in inhibiting the development of posterior and anterior uveitis and has a favorable safety profile in experimental animal models. OphthaliX has submitted a protocol for a Phase II study of uveitis and is currently reviewing its clinical development plans and plans to provide an update on the development for this indication on a later stage.

CF102 for the Treatment of HCC

According to the Living with Liver Cancer HCC is the sixth most common form of cancer, the most common form of liver cancer in adults and the third most common cause of cancer-related mortality worldwide, particularly in Asia. According to the American Cancer Society, more than 700,000 people are diagnosed with liver cancer each year throughout the world and more than 600,000 persons die from liver cancer each year. Nexavar is the only approved drug for HCC and prolongs patient survival time by only a few months. GlobalData recently estimated that in 2017, the HCC market will be $1.2 billion. However, Global Industry Analysts predicts that the market for HCC drugs will increase to approximately $2.0 billion by 2015.

Currently, there is no vaccine for HCC. Several therapies are in advanced clinical development for HCC. Some drugs under development act as a single agent and some act in combination with Nexavar. Moreover, some are first line treatments while others are second line treatments. In addition, many existing approaches are used in the treatment of unresectable liver cancer, including alcohol injection, radiofrequency ablation, chemoembolization, cryoablation and radiation therapy.

CF102 for the Treatment of HCV

According to the U.S. Centers for Disease Control and Prevention, or the CDC, approximately 3.2 million people in the United States have chronic HCV, a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people with HCV have no symptoms of the disease until liver damage occurs, which may take several years. Also according to the CDC, approximately 75% to 85% of persons carrying the HCV will develop a chronic disease, such as liver cancer, liver failure or death. According to Renub Research, the market for HCV drugs is experiencing a dramatic near-term growth, by crossing $6 billion in 2011 and is expected to be more than double of its current figure by 2015. Renub Research believes that the robust growth will be driven primarily by the launch of novel premium-priced agents that will increase the size of the drug-treated population, mainly as a result of the re-treatment of prior non-responder patients.

Currently, there is no vaccine for HCV. Prior to the recent approval of Telaprevir and Boceprevir, the available treatment was a combination of interferon injections and ribavarin pills. Less than 50% of patients respond to this therapy and after some time, patients may develop a resistance to the combination. In addition, these drugs may cause severe side effects. Drugs currently approved for the treatment of HCV include interferon-alpha-based products, ribavirin-based products and protease inhibitors.

There are also several companies that specialize in the development of HCV therapies. The HCV therapies currently in development in multiple classes include protease inhibitors, polymerase inhibitors (nucleoside and non-nucleoside), NS5A inhibitors, toll-like receptor inhibitors and cyclophilin inhibitors.

In our studies of CF102, it has shown a good safety profile and a capability to decrease the viral load in HCV patients that also have HCC. We plan to examine the viral load of HCC patients who are also infected with HCV as part of our next HCC Phase II study.

Insurance

We maintain insurance for our offices and laboratory in Petah-Tikva, Israel. Our insurance program covers approximately $0.375 million of equipment and lease improvements against risk of loss, excluding damage from inventory theft. In addition, we maintain the following insurance: employer liability with coverage of approximately $5.0 million; third party liability with coverage of approximately $0.75 million; fire insurance coverage of approximately $0.725 million; natural disaster coverage of approximately $1.1 million; all risk coverage of approximately $0.02 million for electronic equipment and machinery insurance for laboratory refrigerators; and directors' and officers' liability with coverage of $2.0 million per claim and $10.0 million in the aggregate.

We also maintain worldwide product and clinical trial liability insurance with coverage of approximately $3 million with respect to the CF101 and CF102 drugs used in clinical trials. We also procure additional insurance for each specific clinical trial which covers a certain number of trial participants and which varies based on the particular clinical trial. Certain of such policies are based on the Declaration of Helsinki, which is a set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association, and certain protocols of the Israeli Ministry of Health.

We procure cargo marine coverage when we ship substances for our clinical studies. Such insurance is custom-fit to the special requirements of the applicable shipment, such as temperature and/or climate sensitivity. If required, we insure the substances to the extent they are stored in central depots and at clinical sites.

We believe that our insurance policies are adequate and customary for a business of our kind. However, because of the nature of our business, we cannot assure you that we will be able to maintain insurance on a commercially reasonable basis or at all, or that any future claims will not exceed our insurance coverage.

Environmental Matters

We are subject to various environmental, health and safety laws and regulations, including those governing air emissions, water and wastewater discharges, noise emissions, the use, management and disposal of hazardous, radioactive and biological materials and wastes and the cleanup of contaminated sites. We believe that our business, operations and facilities are being operated in compliance in all material respects with applicable environmental and health and safety laws and regulations. Our laboratory personnel in Israel have ongoing communication with the Israeli Ministry of Environmental Protection in order to verify compliance with relevant instructions and regulations. In addition, all of our laboratory personnel participate in instruction on the proper handling of chemicals, including hazardous substances before commencing employment, and during the course of their employment, with us. In addition, all information with respect to any chemical substance that we use is filed and stored as a Material Safety Data Sheet, as required by applicable environmental regulations. Based on information currently available to us, we do not expect environmental costs and contingencies to have a material adverse effect on us. The operation of our testing facilities, however, entails risks in these areas. Significant expenditures could be required in the future if these facilities are required to comply with new or more stringent environmental or health and safety laws, regulations or requirements. See “Business — Government Regulation and Funding — Israel Ministry of Environment — Toxin Permit.”

Government Regulation and Funding

We operate in a highly controlled regulatory environment. Stringent regulations establish requirements relating to analytical, toxicological and clinical standards and protocols in respect of the testing of pharmaceuticals. Regulations also cover research, development, manufacturing and reporting procedures, both pre- and post-approval. In many markets, especially in Europe, marketing and pricing strategies are subject to national legislation or administrative practices that include requirements to demonstrate not only the quality, safety and efficacy of a new product, but also its cost-effectiveness relating to other treatment options. Failure to comply with regulations can result in stringent sanctions, including product recalls, withdrawal of approvals, seizure of products and criminal prosecution.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through preclinical studies and clinical trials that our product candidates are safe and effective. Historically, the results from preclinical studies and early clinical trials often have not accurately predicted results of later clinical trials. In addition, a number of pharmaceutical products have shown promising results in clinical trials but subsequently failed to establish sufficient safety and efficacy results to obtain necessary regulatory approvals. We have incurred and will continue to incur substantial expense for, and devote a significant amount of time to, preclinical studies and clinical trials. Many factors can delay the commencement and rate of completion of clinical trials, including the inability to recruit patients at the expected rate, the inability to follow patients adequately after treatment, the failure to manufacture sufficient quantities of materials used for clinical trials, and the emergence of unforeseen safety issues and governmental and regulatory delays. If a product candidate fails to demonstrate safety and efficacy in clinical trials, this failure may delay development of other product candidates and hinder our ability to conduct related preclinical studies and clinical trials. Additionally, as a result of these failures, we may also be unable to obtain additional financing.

Governmental authorities in all major markets require that a new pharmaceutical product be approved or exempted from approval before it is marketed, and have established high standards for technical appraisal, which can result in an expensive and lengthy approval process. The time to obtain approval varies by country and some products are never approved. The lengthy process of conducting clinical trials, seeking approval and the subsequent compliance with applicable statutes and regulations, if approval is obtained, are very costly and require the expenditure of substantial resources.

A summary of the U.S., EU and Israeli regulatory processes follow below.

United States

In the United States, the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act, as amended, and the regulations promulgated thereunder, and other federal and state statutes and regulations govern, among other things, the safety and effectiveness standards for our products and the raw materials and components used in the production of, testing, manufacture, labeling, storage, record keeping, approval, advertising and promotion of our products on a product-by-product basis.

Preclinical tests include *in vitro* and *in vivo* evaluation of the product candidate, its chemistry, formulation and stability, and animal studies to assess potential safety and efficacy. Certain preclinical tests must be conducted in compliance with good laboratory practice regulations. Violations of these regulations can, in some cases, lead to invalidation of the studies, requiring them to be replicated. After laboratory analysis and preclinical testing, testing, a sponsor files an Investigational New Drug application, or IND, to begin human testing. Typically, a manufacturer conducts a three-phase human clinical testing program which itself is subject to numerous laws and regulatory requirements, including adequate monitoring, reporting, record keeping and informed consent. In Phase I, small clinical trials are conducted to determine the safety and proper dose ranges of our product candidates. In Phase II, clinical trials are conducted to assess safety and gain preliminary evidence of the efficacy of our product candidates. In Phase III, clinical trials are conducted to provide sufficient data for the statistically valid evidence of safety and efficacy. The time and expense required for us to perform this clinical testing can vary and is substantial. We cannot be certain that we will successfully complete Phase I, Phase II or Phase III testing of our product candidates within any specific time period, if at all. Furthermore, the FDA, the Institutional Review Board responsible for approving and monitoring the clinical trials at a given site, the Data Safety Monitoring Board, where one is used, or we may suspend the clinical trials at any time on various grounds, including a finding that subjects or patients are exposed to unacceptable health risk.

If the clinical data from these clinical trials (Phases I, II and III) are deemed to support the safety and effectiveness of the candidate product for its intended use, then we may proceed to seek to file with the FDA, a New Drug Application, or NDA, seeking approval to market a new drug for one or more specified intended uses. We have not completed our clinical trials for any candidate product for any intended use and therefore, we cannot ascertain whether the clinical data will support and justify filing an NDA. Nevertheless, if and when we are able to ascertain that the clinical data supports and justifies filing an NDA, we intend to make such appropriate filings.

The purpose of the NDA is to provide the FDA with sufficient information so that it can assess whether it ought to approve the candidate product for marketing for specific intended uses. The fact that the FDA has designated a drug as an orphan drug for a particular intended use does not mean that the drug has been approved for marketing. Only after an NDA has been approved by the FDA is marketing appropriate. A request for orphan drug status must be filed before the NDA is filed. The orphan drug designation, though, provides certain benefits, including a seven-year period of market exclusivity subject to certain exceptions. In February 2012, the FDA granted an orphan drug status for the active moiety, or the part of the drug that is responsible for the physiological or pharmacological action of the drug substance, of CF102 for the treatment of HCC. See “Item 4. Information on the Company—B. Business Overview—CF102”.

The NDA normally contains, among other things, sections describing the chemistry, manufacturing, and controls, non-clinical pharmacology and toxicology, human pharmacokinetics and bioavailability, microbiology, the results of the clinical trials, and the proposed labeling which contains, among other things, the intended uses of the candidate product.

We cannot take any action to market any new drug or biologic product in the United States until our appropriate marketing application has been approved by the FDA. The FDA has substantial discretion over the approval process and may disagree with our interpretation of the data submitted. The process may be significantly extended by requests for additional information or clarification regarding information already provided. As part of this review, the FDA may refer the application to an appropriate advisory committee, typically a panel of clinicians. Satisfaction of these and other regulatory requirements typically takes several years, and the actual time required may vary substantially based upon the type, complexity and novelty of the product. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures on our activities. We cannot be certain that the FDA or other regulatory agencies will approve any of our products on a timely basis, if at all. Success in preclinical or early stage clinical trials does not assure success in later-stage clinical trials. Even if a product receives regulatory approval, the approval may be significantly limited to specific indications or uses and these limitations may adversely affect the commercial viability of the product. Delays in obtaining, or failures to obtain regulatory approvals, would have a material adverse effect on our business.

Even after we obtain FDA approval, we may be required to conduct further clinical trials (i.e., Phase IV trials) and provide additional data on safety and effectiveness. We are also required to gain separate approval for the use of an approved product as a treatment for indications other than those initially approved. In addition, side effects or adverse events that are reported during clinical trials can delay, impede or prevent marketing approval. Similarly, adverse events that are reported after marketing approval can result in additional limitations being placed on the product's use and, potentially, withdrawal of the product from the market. Any adverse event, either before or after marketing approval, can result in product liability claims against us.

As an alternate path for FDA approval of new indications or new formulations of previously-approved products, a company may file a Section 505(b)(2) NDA, instead of a "stand-alone" or "full" NDA. Section 505(b)(2) of the Food, Drug, and Cosmetic Act, or FDC, was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, otherwise known as the Hatch-Waxman Amendments. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Some examples of products that may be allowed to follow a 505(b)(2) path to approval are drugs that have a new dosage form, strength, route of administration, formulation or indication. The Hatch-Waxman Amendments permit the applicant to rely upon certain published nonclinical or clinical studies conducted for an approved product or the FDA's conclusions from prior review of such studies. The FDA may require companies to perform additional studies or measurements to support any changes from the approved product. The FDA may then approve the new product for all or some of the labeled indications for which the reference product has been approved, as well as for any new indication supported by the NDA. While references to nonclinical and clinical data not generated by the applicant or for which the applicant does not have a right of reference are allowed, all development, process, stability, qualification and validation data related to the manufacturing and quality of the new product must be included in an NDA submitted under Section 505(b)(2).

To the extent that the Section 505(b)(2) applicant is relying on the FDA's conclusions regarding studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book publication. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The Section 505(b)(2) application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the reference product has expired. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its products only to be subject to significant delay and patent litigation before its products may be commercialized.

In addition to regulating and auditing human clinical trials, the FDA regulates and inspects equipment, facilities, laboratories and processes used in the manufacturing and testing of such products prior to providing approval to market a product. If after receiving FDA approval, we make a material change in manufacturing equipment, location or process, additional regulatory review and approval may be required. We also must adhere to cGMP regulations and product-specific regulations enforced by the FDA through its facilities inspection program. The FDA also conducts regular, periodic visits to re-inspect our equipment, facilities, laboratories and processes following the initial approval. If, as a result of these inspections, the FDA determines that our equipment, facilities, laboratories or processes do not comply with applicable FDA regulations and conditions of product approval, the FDA may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of our manufacturing operations.

We have currently received no approvals to market our products from the FDA or other foreign regulators.

We are also subject to various federal, state and international laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws. The federal Anti-kickback law, which governs federal healthcare programs (e.g., Medicare, Medicaid), makes it illegal to solicit, offer, receive or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Many states have similar laws that are not restricted to federal healthcare programs. Federal and state false claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third party payers (including Medicare and Medicaid), claims for reimbursement, including claims for the sale of drugs or services, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. If the government or a whistleblower were to allege that we violated these laws there could be a material adverse effect on us, including our stock price. Even an unsuccessful challenge could cause adverse publicity and be costly to respond to, which could have a materially adverse effect on our business, results of operations and financial condition. A finding of liability under these laws can have significant adverse financial implications for us and can result in payment of large penalties and possible exclusion from federal healthcare programs. We will consult counsel concerning the potential application of these and other laws to our business and our sales, marketing and other activities and will make good faith efforts to comply with them. However, given their broad reach and the increasing attention given by law enforcement authorities, we cannot assure you that some of our activities will not be challenged or deemed to violate some of these laws.

European Economic Area

Although we are not currently seeking regulatory approval in the EU, we or our licensees may do so in the future. As such, a summary of the EU regulatory processes follows below.

A medicinal product may only be placed on the market in the European Economic Area, or EEA, composed of the 27 EU member states, plus Norway, Iceland and Lichtenstein, when a marketing authorization has been issued by the competent authority of a member state pursuant to Directive 2001/83/EC (as recently amended by Directive 2004/27/EC), or an authorization has been granted under the centralized procedure in accordance with Regulation (EC) No. 726/2004 or its predecessor, Regulation 2309/93. There are essentially three community procedures created under prevailing European pharmaceutical legislation that, if successfully completed, allow an applicant to place a medicinal product on the market in the EEA.

Centralized Procedure

Regulation 726/2004/EC now governs the centralized procedure when a marketing authorization is granted by the European Commission, acting in its capacity as the European Licensing Authority on the advice of the EMA. That authorization is valid throughout the entire community and directly or (as to Norway, Iceland and Liechtenstein) indirectly allows the applicant to place the product on the market in all member states of the EEA. The EMA is the administrative body responsible for coordinating the existing scientific resources available in the member states for evaluation, supervision and pharmacovigilance of medicinal products. Certain medicinal products, as described in the Annex to Regulation 726/2004, must be authorized centrally. These are products that are developed by means of a biotechnological process in accordance with Paragraph 1 to the Annex to the Regulation. Medicinal products for human use containing a new active substance for which the therapeutic indication is the treatment of acquired immune deficiency syndrome, or AIDS, cancer, neurodegenerative disorder or diabetes must also be authorized centrally. Starting on May 20, 2008, the mandatory centralized procedure was extended to autoimmune diseases and other immune dysfunctions and viral diseases. Finally, all medicinal products that are designated as orphan medicinal products pursuant to Regulation 141/2000 must be authorized under the centralized procedure. An applicant may also opt for assessment through the centralized procedure if it can show that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization centrally is in the interests of patients at the community level. For each application submitted to the EMA for scientific assessment, the EMA is required to ensure that the opinion of the Committee for Medicinal Products for Human Use, or CHMP, is given within 210 days after receipt of a valid application. This 210 days period does not include the time that the applicant to answer any questions raised during the application procedure, the so-called 'clock stop' period. If the opinion is positive, the EMA is required to send the opinion to the European Commission, which is responsible for preparing the draft decision granting a marketing authorization. This draft decision may differ from the CHMP opinion, stating reasons for diverging for the CHMP opinion. The draft decision is sent to the applicant and the member states, after which the European Commission takes a final decision. If the initial opinion of the CHMP is negative, the applicant is afforded an opportunity to seek a re-examination of the opinion. The CHMP is required to re-examine its opinion within 60 days following receipt of the request by the applicant. All CHMP refusals and the reasons for refusal are made public on the EMA website. Without a centralized marketing authorization it is prohibited to place a medicinal product that must be authorized centrally on the market in the EU.

Mutual Recognition and Decentralized Procedures

With the exception of products that are authorized centrally, the competent authorities of the member states are responsible for granting marketing authorizations for medicinal products placed on their national markets. If the applicant for a marketing authorization intends to market the same medicinal product in more than one member state, the applicant may seek an authorization progressively in the community under the mutual recognition or decentralized procedure. Mutual recognition is used if the medicinal product has already been authorized in a member state. In this case, the holder of this marketing authorization requests the member state where the authorization has been granted to act as reference member state by preparing an updated assessment report that is then used to facilitate mutual recognition of the existing authorization in the other member states in which approval is sought (the so-called concerned member state(s)). The reference member state must prepare an updated assessment report within 90 days of receipt of a valid application. This report together with the approved Summary of Product Characteristics, or SmPC (which sets out the conditions of use of the product), and a labeling and package leaflet are sent to the concerned member states for their consideration. The concerned member states are required to approve the assessment report, the SmPC and the labeling and package leaflet within 90 days of receipt of these documents. The total procedural time is 180 days.

The decentralized procedure is used in cases where the medicinal product has not received a marketing authorization in the EU at the time of application. The applicant requests a member state of its choice to act as reference member state to prepare an assessment report that is then used to facilitate agreement with the concerned member states and the grant of a national marketing authorization in all of these member states. In this procedure, the reference member state must prepare, for consideration by the concerned member states, the draft assessment report, a draft SmPC and a draft of the labeling and package leaflet within 120 days after receipt of a valid application. As in the case of mutual recognition, the concerned member states are required to approve these documents within 90 days of their receipt.

For both mutual recognition and decentralized procedures, if a concerned member state objects to the grant of a marketing authorization on the grounds of a potential serious risk to public health, it may raise a reasoned objection with the reference member state. The points of disagreement are in the first instance referred to the Co-ordination Group on Mutual Recognition and Decentralized Procedures, or CMD, to reach an agreement within 60 days of the communication of the points of disagreement. If member states fail to reach an agreement, then the matter is referred to the EMA and CHMP for arbitration. The CHMP is required to deliver a reasoned opinion within 60 days of the date on which the matter is referred. The scientific opinion adopted by the CHMP forms the basis for a binding European Commission decision.

Irrespective of whether the medicinal product is assessed centrally, de-centrally or through a process of mutual recognition, the medicinal product must be manufactured in accordance with the principles of good manufacturing practice as set out in Directive 2003/94/EC and Volume 4 of the rules governing medicinal products in the European community. Moreover, community law requires the clinical results in support of clinical safety and efficacy based upon clinical trials conducted in the European community to be in compliance with the requirements of Directive 2001/20/EC, which implements good clinical practice in the conduct of clinical trials on medicinal products for human use. Clinical trials conducted outside the European community and used to support applications for marketing within the EU must have been conducted in a way consistent with the principles set out in Directive 2001/20/EC. The conduct of a clinical trial in the EU requires, pursuant to Directive 2001/20/EC, authorization by the relevant national competent authority where a trial takes place, and an ethics committee to have issued a favorable opinion in relation to the arrangements for the trial. It also requires that the sponsor of the trial, or a person authorized to act on his behalf in relation to the trial, be established in the community.

National Procedure

This procedure is available for medicinal products that do not fall within the scope of mandatory centralized authorization and are intended for use in only one EU member state. Specific procedures and timelines differ between member states, but the duration of the procedure is generally 210 days and based on a risk/efficacy assessment by the competent authority of the member state concerned, followed by determination of SmPC, package leaflet and label text/layout and subsequently grant of the marketing authorization. Marketing authorizations granted on this basis are not mutually recognized by other member states.

There are various types of applications for marketing authorizations:

Full Applications. A full application is one that is made under any of the community procedures described above and "stands alone" in the sense that it contains all of the particulars and information required by Article 8(3) of Directive 2001/83 (as amended) to allow the competent authority to assess the quality, safety and efficacy of the product and in particular the balance between benefit and risk. Article 8(3)(l) in particular refers to the need to present the results of the applicant's research on (i) pharmaceutical (physical-chemical, biological or microbiological) tests, (ii) preclinical (toxicological and pharmacological) studies and (iii) clinical trials in humans. The nature of these tests, studies and trials is explained in more detail in Annex I to Directive 2001/83/EC. Full applications would be required for products containing new active substances not previously approved by the competent authority, but may also be made for other products.

Abridged Applications. Article 10 of Directive 2001/83/EC contains exemptions from the requirement that the applicant provide the results of its own preclinical and clinical research. There are three regulatory routes for an applicant to seek an exemption from providing such results, namely (i) cross-referral to an innovator's results without consent of the innovator, (ii) well established use according to published literature and (iii) consent to refer to an existing dossier of research results filed by a previous applicant.

Cross-referral to Innovator's Data

Articles 10(1) and 10(2)(b) of Directive 2001/83/EC provide the legal basis for an applicant to seek a marketing authorization on the basis that its product is a generic medicinal product (a copy) of a reference medicinal product that has already been authorized, in accordance with community provisions. A reference product is, in principle, an original product granted an authorization on the basis of a full dossier of particulars and information. This is the main exemption used by generic manufacturers for obtaining a marketing authorization for a copy product. The generic applicant is not required to provide the results of preclinical studies and of clinical trials if its product meets the definition of a generic medicinal product and the applicable regulatory results protection period for the results submitted by the innovator has expired. A generic medicinal product is defined as a medicinal product:

- having the same qualitative and quantitative composition in active substance as the reference medicinal product;
- having the same pharmaceutical form as the reference medicinal product; and
- whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

Applications in respect of a generic medicinal product cannot be made before the expiry of the protection period. Where the reference product was granted a national marketing authorization pursuant to an application made before October 30, 2005, the protection period is either 6 years or 10 years, depending upon the election of the particular member state concerned. Where the reference product was granted a marketing authorization centrally, pursuant to an application made before November 20, 2005, the protection period is 10 years. For applications made after these dates, Regulation 726/2004 and amendments to Directive 2001/83/EC provide for a harmonized protection period regardless of the approval route utilized. The harmonized protection period is in total 10 years, including eight years of research data protection and two years of marketing protection. The effect is that the originator's results can be the subject of a cross-referral application after eight years, but any resulting authorization cannot be exploited for a further two years. The rationale of this procedure is not that the competent authority does not have before it relevant tests and trials upon which to assess the efficacy and safety of the generic product, but that the relevant particulars can, if the research data protection period has expired, be found on the originator's file and used for assessment of the generic medicinal product. The 10-year protection period can be extended to 11 years where, in the first eight years post-authorization, the holder of the authorization obtains approval for a new indication assessed as offering a significant clinical benefit in comparison with existing products.

If the copy product does not meet the definition of a generic medicinal product or if certain types of changes occur in the active substance(s) or in the therapeutic indications, strength, pharmaceutical form or route of administration in relation to the reference medicinal product, Article 10(3) of Directive 2001/83/EC provides that the results of the appropriate preclinical studies or clinical trials must be provided by the applicant.

Well-established Medicinal Use

Under Article 10a of Directive 2001/83/EC, an applicant may, in substitution for the results of its own preclinical and clinical research, present detailed references to published literature demonstrating that the active substance(s) of a product have a well-established medicinal use within the community with recognized efficacy and an acceptable level of safety. The applicant is entitled to refer to a variety of different types of literature, including reports of clinical trials with the same active substance(s) and epidemiological studies that indicate that the constituent or constituents of the product have an acceptable safety/efficacy profile for a particular indication. However, use of the published literature exemption is restricted by stating that in no circumstances will constituents be treated as having a well-established use if they have been used for less than 10 years from the first systematic and documented use of the substance as a medicinal product in the EU. Even after 10 years' systematic use, the threshold for well-established medicinal use might not be met. European pharmaceutical law requires the competent authorities to consider among other factors the period over which a substance has been used, the amount of patient use of the substance, the degree of scientific interest in the use of the substance (as reflected in the scientific literature) and the coherence (consistency) of all the scientific assessments made in the literature. For this reason, different substances may reach the threshold for well-established use after different periods, but the minimum period is 10 years. If the applicant seeks approval of an entirely new therapeutic use compared with that to which the published literature refers, additional preclinical and/or clinical results would have to be provided.

Informed Consent

Under Article 10c of Directive 2001/83/EC, following the grant of a marketing authorization the holder of such authorization may consent to a competent authority utilizing the pharmaceutical, preclinical and clinical documentation that it submitted to obtain approval for a medicinal product to assess a subsequent application relating to a medicinal product possessing the same qualitative and quantitative composition with respect to the active substances and the same pharmaceutical form.

Law Relating to Pediatric Research

Regulation (EC) 1901/2006 (as amended by Regulation (EC) 1902/2006) was adopted on December 12, 2006. This Regulation governs the development of medicinal products for human use in order to meet the specific therapeutic needs of the pediatric population. It requires any application for marketing authorization made after July 26, 2008 in respect of a product not authorized in the European Community on January 26, 2007 (the time the Regulation entered into force), to include the results of all studies performed and details of all information collected in compliance with a pediatric investigation plan agreed by the Pediatric Committee of the EMA, unless the product is subject to an agreed waiver or deferral or unless the product is excluded from the scope of Regulation 1902/2006 (generics, hybrid medicinal products, biosimilars, homeopathic and traditional (herbal) medicinal products and medicinal products containing one or more active substances of well-established medicinal use). Waivers can be granted in certain circumstances where pediatric studies are not required or desirable. Deferrals can be granted in certain circumstances where the initiation or completion of pediatric studies should be deferred until appropriate studies in adults have been performed. Moreover, this regulation imposes the same obligation from January 26, 2009 on an applicant seeking approval of a new indication, pharmaceutical form or route of administration for a product already authorized and still protected by a supplementary protection certificate granted under Regulation EC 469/2009 and its precursor (EEC) 1768/92 or by a patent that qualifies for the granting of such a supplementary protection certificate. The pediatric Regulation 1901/2006 also provides, subject to certain conditions, a reward for performing such pediatric studies, regardless of whether the pediatric results provided resulted in the grant of a pediatric indication. This reward comes in the form of an extension of six months to the supplementary protection certificate granted in respect of the product, unless the product is subject to orphan drug designation, in which case the 10-year market exclusivity period for such orphan products is extended to 12 years. If any of the non-centralized procedures for marketing authorization have been used, the six-month extension of the supplementary protection certificate is only granted if the medicinal product is authorized in all member states.

Post-authorization Obligations

In the pre-authorization phase the applicant must provide a detailed pharmacovigilance plan that it intends to implement post-authorization. An authorization to market a medicinal product in the EU carries with it an obligation to comply with many post-authorization organizational and behavioral regulations relating to the marketing and other activities of authorization holders. These include requirements relating to post-authorization efficacy studies, post-authorization safety studies, adverse event reporting and other pharmacovigilance requirements, advertising, packaging and labeling, patient package leaflets, distribution and wholesale dealing. The regulations frequently operate within a criminal law framework and failure to comply with the requirements may not only affect the authorization, but also can lead to financial and other sanctions levied on the company in question and responsible officers. As a result of the currently on-going overhaul of EU pharmacovigilance legislation the financial and organizational burden on market authorization holders will increase significantly, such as the obligation to maintain a pharmacovigilance system master file that applies to all holders of marketing authorizations granted in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004. Marketing authorization holders must furthermore collect data on adverse events associated with use of the authorized product outside the scope of the authorization. Pharmacovigilance for biological products and medicines with a new active substance will be strengthened by subjecting their authorization to additional monitoring activities. The EU is currently in the process of issuing implementing regulations for the new pharmacovigilance framework.

Any authorization granted by member state authorities, which within three years of its granting is not followed by the actual placing on the market of the authorized product in the authorizing member state ceases to be valid. When an authorized product previously placed on the market in the authorizing member state is no longer actually present on the market for a period of three consecutive years, the authorization for that product shall cease to be valid. The same two three year periods apply to authorizations granted by the European Commission based on the centralized procedure.

Israel

Israel Ministry of the Environment — Toxin Permit

In accordance with the Israeli Dangerous Substance Law — 1993, the Ministry of the Environment may grant a permit in order to use toxic materials. Because we utilize toxic materials in the course of operation of our laboratories, we were required to apply for a permit to use these materials. Our current toxin permit will remain in effect until January 2017.

Other Licenses and Approvals

We have a business license from the municipality of Petah-Tikva for a drug development research laboratory located at our offices in Petah Tikva, Israel. In order to obtain this license, we also received approval from the Petah-Tikva Association of Towns Fire Department. The business license is valid until December 2017. We also have a radioactive materials or products containing radioactive materials license, which is valid until July 2017.

In 2002, we received approval from the National Council on Animal Experiments, approving us as an institution authorized to conduct experiments on animals.

Clinical Testing in Israel

In order to conduct clinical testing on humans in Israel, special authorization must first be obtained from the ethics committee and general manager of the institution in which the clinical studies are scheduled to be conducted, as required under the Guidelines for Clinical Trials in Human Subjects implemented pursuant to the Israeli Public Health Regulations (Clinical Trials in Human Subjects), as amended from time to time, and other applicable legislation. These regulations also require authorization from the Israeli Ministry of Health, except in certain circumstances, and in the case of genetic trials, special fertility trials and similar trials, an additional authorization of the overseeing institutional ethics committee. The institutional ethics committee must, among other things, evaluate the anticipated benefits that are likely to be derived from the project to determine if it justifies the risks and inconvenience to be inflicted on the human subjects, and the committee must ensure that adequate protection exists for the rights and safety of the participants as well as the accuracy of the information gathered in the course of the clinical testing. Since we intend to perform a portion of the clinical studies on certain of our product candidates in Israel, we will be required to obtain authorization from the ethics committee and general manager of each institution in which we intend to conduct our clinical trials, and in most cases, from the Israeli Ministry of Health.

Israel Ministry of Health

Israel's Ministry of Health, which regulates medical testing, has adopted protocols that correspond, generally, to those of the FDA and the EMA, making it comparatively straightforward for studies conducted in Israel to satisfy FDA and the European Medicines Agency requirements, thereby enabling medical technologies subjected to clinical trials in Israel to reach U.S. and EU commercial markets in an expedited fashion. Many members of Israel's medical community have earned international prestige in their chosen fields of expertise and routinely collaborate, teach and lecture at leading medical centers throughout the world. Israel also has free trade agreements with the United States and the European Union.

Other Countries

In addition to regulations in the United States, the EU and Israel, we are subject to a variety of other regulations governing clinical trials and commercial sales and distribution of drugs in other countries. Whether or not our products receive approval from the FDA, approval of such products must be obtained by the comparable regulatory authorities of countries other than the United States before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials and product licensing vary greatly from country to country.

The requirements that we and our collaborators must satisfy to obtain regulatory approval by government agencies in other countries prior to commercialization of our products in such countries can be rigorous, costly and uncertain. In Canada and Australia, regulatory requirements and approval processes are similar in principle to those in the United States. For example, in Canada, pharmaceutical product candidates are regulated by the Food and Drugs Act and the rules and regulations promulgated thereunder, which are enforced by the Therapeutic Products Directorate of Health Canada, or Health Canada. Before commencing clinical trials in Canada, an applicant must complete preclinical studies and file a clinical trial application with Health Canada. After filing a clinical trial application, the applicant must receive different clearance authorizations to proceed with Phase 1 clinical trials, which can then lead to Phase 2 and Phase 3 clinical trials. To obtain regulatory approval to commercialize a new drug in Canada, a new drug submission, or NDS, must be filed with Health Canada. If the NDS demonstrates that the product was developed in accordance with the regulatory authorities' rules, regulations and guidelines and demonstrates favorable safety and efficacy and receives a favorable risk/benefit analysis, Health Canada issues a notice of compliance which allows the applicant to market the product. Facilities, procedures, operations and/or testing of products are subject to periodic inspection by Health Canada and the Health Products and Food Branch Inspectorate. In addition, Health Canada conducts pre-approval and post-approval reviews and plant inspections to determine whether systems are in compliance with the good manufacturing practices in Canada, Drug Establishment Licensing requirements and other provisions of the Food and Drug Regulations.

Foreign governments also have stringent post-approval requirements including those relating to manufacture, labeling, reporting, record keeping and marketing. Failure to substantially comply with these on-going requirements could lead to government action against the product, our company and/or our representatives.

Although we are not currently conducting research and development activities in certain Asian countries, including Korea and Japan, certain of our licensees, KD and SKK, are conducting such activities with respect to CF101 in those countries, respectively. Any regulatory approval process that may impact such licensees' ability to continue their activities or obtain regulatory approval in those countries could impact the revenues we generate from our out-licensing agreements with them.

Related Matters

From time to time, legislation is drafted, introduced and passed in governmental bodies that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA, EMA, the Israeli Ministry of Health and other applicable regulatory bodies to which we are subject. In addition, regulations and guidance are often revised or reinterpreted by the national agency in ways that may significantly affect our business and our product candidates. It is impossible to predict whether such legislative changes will be enacted, whether FDA, EMA or Israeli Ministry of Health regulations, guidance or interpretations will change, or what the impact of such changes, if any, may be. We may need to adapt our business and product candidates and products to changes that occur in the future.

C. Organizational Structure

Our corporate structure consists of Can-Fite and three subsidiaries, one of which is an indirect subsidiary: Ultratrend Limited, an English limited company, OphthaliX Inc., a Delaware corporation, or OphthaliX, and Eye-Fite Limited, an Israeli limited company, or Eye-Fite. Ultratrend Limited is a wholly-owned subsidiary of Can-Fite, but has yet to conduct any significant activity. Can-Fite holds 82% of the issued and outstanding capital stock of OphthaliX and accordingly may appoint all members of the Board of Directors of OphthaliX. Eye-Fite, a wholly-owned subsidiary of OphthaliX, holds an exclusive license from Can-Fite, pursuant to which OphthaliX develops CF101 for use in the ophthalmic field.

D. Property, Plants and Equipment.

We are headquartered in Petah-Tikva, Israel. We lease one floor in one facility pursuant to a lease agreement with Eshkolit Nihul Nadlan LTD, an Israeli limited company, that pursuant to a verbal agreement expires on December 31, 2015.The Petah-Tikva headquarters consists of approximately 300 square meters of space with eight parking spaces. Lease payments are approximately NIS 20,448, or $5,665, per month. If our lease is terminated, we do not foresee significant difficulty in leasing another suitable facility. The current facility houses both our administrative, clinical and research operations. The research laboratory consists of approximately 150 square meters and includes a tissue culture laboratory and a molecular biology laboratory.

ITEM 4A. Unresolved Staff Comments

Not Applicable.

ITEM 5. Operating and Financial Review and Prospects

The information in this section should be read in conjunction with our consolidated financial statements and related notes beginning on page F-1 and the related information included elsewhere in this Annual Report on Form 20-F. Our financial statements are prepared in accordance with IFRS as issued by the International Accounting Standards Board, and reported in NIS. We maintain our accounting books and records in NIS and our functional currency is NIS. Certain amounts presented herein may not sum due to rounding.

Overview

We are a clinical-stage biopharmaceutical company focused on developing orally bioavailable small molecule therapeutic products for the treatment of autoimmune-inflammatory, oncological and ophthalmic diseases. Our platform technology utilizes the Gi protein associated A3AR as a therapeutic target. A3AR is highly expressed in inflammatory and cancer cells, and not significantly expressed in normal cells, suggesting that the receptor could be a unique target for pharmacological intervention. Our pipeline of drug candidates are synthetic, highly specific agonists and allosteric modulators, or ligands or molecules that initiate molecular events when binding with target proteins, targeting the A3AR. Our strategy is to build a fully integrated biotechnology company that discovers, in-licenses and develops an innovative and effective small molecule drug portfolio of ligands that bind to a specific therapeutic target for the treatment of autoimmune-inflammatory, oncological, ophthalmic diseases and more. We continue to develop and test our existing pipeline, while also testing other indications for our existing drug candidates and examining, from time to time, the potential of other small molecules that may fit our platform technology of utilizing small molecules to target the A3AR. We generally focus on drugs with global market potential and we seek to create global partnerships to effectively assist us in developing our portfolio and to market our products.

We have in-licensed three different A3AR ligands which represent our current pipeline of drug candidates under development and include two synthetic A3AR agonists, CF101 (known generically as IB-MECA) and CF102 (known generically as CI-IB-MECA) from NIH, and an allosteric modulator at the A3AR, CF602 from Leiden University. See “Item 4. Information on the Company—Business Overview—In-Licensing Agreements”. In addition, we have out-licensed CF101 for (i) the treatment of autoimmune diseases to SKK for the Japanese market, (ii) for the treatment of RA to KD for the Korean market and (iii) for the treatment of ophthalmic diseases to Eye-Fite, a wholly-owned subsidiary of OphthaliX for the global market. We also recently entered into a distribution agreement for the distribution of CF101 for the treatment of psoriasis and RA to Cipher for the Canadian market.See “Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements”.

Our drug candidates, CF101, CF102 and CF602 are being developed to treat several autoimmune-inflammatory, oncological and ophthalmic indications. CF101 is in various stages of clinical development for the treatment of autoimmune-inflammatory diseases, including RA, psoriasis, and OA. CF101 is also being developed by OphthaliX for the treatment of ophthalmic indications, including DES, glaucoma and uveitis. The CF102 drug candidate is being developed for the treatment of HCC and for the treatment of HCV. CF602 is our second generation allosteric drug candidate for the treatment of inflammatory diseases, which has shown proof of concept in *in vitro* and *in vivo* studies. In addition, we recently announced that we are planning to develop CF602 to treat sexual dysfunction. Preclinical studies revealed that our drug candidates have potential to treat additional inflammatory diseases, such as Crohn’s disease, oncological diseases and viral diseases, such as the JC virus.

We are currently: (i) expecting top-line results for a recently completed Phase II/III trial with respect to the development of CF101 for the treatment of psoriasis; (ii) preparing for a Phase III trial with respect to the development of CF101 for the treatment of RA; (iii) preparing for a Phase II study with respect to the development of CF101 for the treatment of OA; (iv) conducting a Phase II study with respect to the development of CF102 for the treatment of HCC (and as part of this study, we will also test CF102 in patients with both HCC and HCV); and (v) preparing for further preclinical work with respect to the development of CF602. OphthaliX is currently: (i) conducting a Phase II trial with respect to the development of CF101 for the treatment of glaucoma or related syndromes of ocular hypertension; and (ii) initiating a Phase II study of CF101 for the treatment of uveitis.

Since inception, we have incurred significant losses in connection with our research and development. At December 31, 2014, we had an accumulated deficit of approximately NIS304,150. Although we have begun to recognize revenues in connection with our out-licensing agreements with SKK, KD and OphthaliX, we expect to generate losses in connection with the research and development activities relating to our pipeline of drug candidates. Such research and development activities are budgeted to expand over time and will require further resources if we are to be successful. As a result, we expect to incur operating losses, which may be substantial over the next several years, and we will need to obtain additional funds to further develop or research and development programs.

We have funded our operations primarily through the sale of equity securities (both in private placements and in public offerings) and payments received under the licensing arrangements with SKK and KD. We expect to continue to fund our operations over the next several years through our existing cash resources, potential future milestone payments that we expect to receive from our licensees, interest earned on our investments, if any, and additional capital to be raised through public or private equity offerings or debt financings. As of December 31, 2014, we had approximately $9,280, or NIS36,091, of cash and cash equivalents based on the exchange rate reported by the Bank of Israel as of December 31, 2014.

Revenues

Our revenues to date have been generated primarily from payments under our licensing arrangements with SKK and KD. Under the Seikagaku Agreement, we are entitled to up-front and milestone payments of up to $17million (of which $2 million is attributable to our participation in certain research and development activities), annual payments of $0.5 million, and up to an additional $4 million in milestone payments if SKK pursues a second indication (the current indication is RA). We will also be entitled to royalties in an amount between 7-12% of annual net sales in Japan subject to certain sales criteria. In accordance with the Seikagaku Agreement, we received an up-front payment of $3.0 million in 2006, a milestone payment of $1.0 million in 2008 and $0.5 million per year from 2007 through 2011 as an annual minimum royalty payment (for an aggregate of $2.5 million). Under the Kwang Dong Agreement, we are entitled to up-front and milestone payments of up to $1.5 million. In accordance with the Kwang Dong Agreement, we received an up-front paymentof $0.3 million and a payment of $0.048 million as consideration for KD's purchase of our ordinary shares in 2009 and a milestone payment of $0.2 million in 2010. See "Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements".

Under the terms of the Seikagaku Agreement and the Kwang Dong Agreement, in addition to the payments mentioned above, we are entitled to certain additional payments based on the sale of raw materials, subject to the terms and conditions of the respective agreements. See "Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements". Certain payments we have received from SKK and KD have been subject to a 10% and 5% withholding tax in Japan and Korea, respectively, and certain payments we may receive in the future, if at all, may also be subject to the same withholding tax in Japan and Korea. Receipt of any milestone payment under our out-licensing agreements depends on many factors, some of which are beyond our control. We cannot assure you that we will receive any of these future payments. We expect our revenues for the next several years,if any,to be derived primarily from payments under our current out-license agreements and our public capital raising activities, as well as additional collaborations that we may enter into in the future with respect to our drug candidates.

Research and Development

Our research and development expenses consist primarily of salaries and related personnel expenses, fees paid to external service providers, up-front and milestone payments under our license agreements, patent-related legal fees, costs of preclinical studies and clinical trials, drug and laboratory supplies and costs for facilities and equipment. We charge all research and development expenses to operations as they are incurred. We expect our research and development expense to remain our primary expense in the near future as we continue to develop our products. Increases or decreases in research and development expenditures are attributable to the number and/or duration of the pre-clinical and clinical studies that we conduct.

The following table identifies our current major research and development projects:

Project	Status	Expected or Recent Near Term Milestone
CF 101	Preparing for a Phase III study in RA	Completion of preparatory work for Phase III study
	Ongoing Phase II/III in Psoriasis	Top line results are expected in the end of March 2015
	Ongoing Phase II in Glaucoma (via OphthaliX)	Top line results are expected in Q4 2015
	Preparing for Phase II in Uveitis (via OphthaliX)	Completion of preparatory work for Phase II study
	Preparing for a Phase II in OA	Completion of preparatory work for Phase II study
CF 102	Phase II in HCC	Completion of patient enrollment by end of 2015
CF 602	Pre-Clinical Stage	Continuing pre-clinical studies and preparations

We record certain costs for each development project on a "direct cost" basis, as they are recorded to the project for which such costs are incurred. Such costs include, but are not limited to, CRO expenses, drug production for pre-clinical and clinical studies and other pre-clinical and clinical expenses. However, certain other costs, including but not limited to, salary expenses (including salaries for research and development personnel), facilities, depreciation, share-based compensation and other overhead costs are recorded on an "indirect cost" basis, i.e., they are shared among all of our projects and are not recorded to the project for which such costs are incurred. We do not allocate direct salaries to projects due to the fact that our project managers are generally involved in several projects at different stages of development, and the related salary expense is not significant to the overall cost of the applicable projects. In addition, indirect labor costs relating to our support of the research and development process, such as manufacturing, controls, pre-clinical analysis, laboratory testing and initial drug sample production, as well as rent and other administrative overhead costs, are shared by many different projects and have never been considered by management to be of significance in its decision-making process with respect to any specific project. Accordingly, such costs have not been specifically allocated to individual projects.

Set forth below is a summary of the gross direct costs allocated to our main projects on an individual basis, as well as the gross direct costs allocated to our less significant projects on an aggregate basis, for the years ended December 31, 2012, 2013 and 2014; and on an aggregate basis since project inception:

	(USD in thousands) Year Ended December 31,			Total Costs Since Project
	2012	**2013**	**2014**	**Inception**
CF101	1,987	2,624	1,866	20,274
CF102	15	268	1,289	2,677
CF602	-	-	23	23
Other projects	-	-	18	18
Total gross direct project costs [(1)]	2,002	2,892	3,196	22,992

(1) Does not include indirect project costs and overhead, such as payroll and related expenses (including stock-based compensation), facilities, depreciation and impairment of intellectual property, which are included in total research and development expenses in our financial statements.

Under our licensing agreement with Eye-Fite, Eye-Fite is responsible for making payments to our licensor, the NIH, for certain patent rights relating to CF101. See "Item 10. Additional Information — Material Contracts — Out-Licensing and Distribution Agreements— Eye-Fite Agreement".

From our inception through December 31, 2014, we have incurred research and development expenses of approximately $57million. We expect that a large percentage of our research and development expense in the future will be incurred in support of our current and future preclinical and clinical development projects. Due to the inherently unpredictable nature of preclinical and clinical development processes and given the early stage of our preclinical product development projects, we are unable to estimate with any certainty the costs we will incur in the continued development of the product candidates in our pipeline for potential commercialization. Clinical development timelines, the probability of success and development costs can differ materially from expectations. We expect to continue to test our product candidates in preclinical studies for toxicology, safety and efficacy, and to conduct additional clinical trials for each product candidate. If we are not able to enter into an out-licensing arrangement with respect to any product candidate prior to the commencement of later stage clinical trials, we may fund the trials for the product candidates ourselves.

While we are currently focused on advancing each of our product development projects, our future research and development expenses will depend on the clinical success of each product candidate, as well as ongoing assessments of each product candidate's commercial potential. In addition, we cannot forecast with any degree of certainty which product candidates may be subject to future out-licensing arrangements, when such out-licensing arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

As we obtain results from clinical trials, we may elect to discontinue or delay clinical trials for certain product candidates or projects in order to focus our resources on more promising product candidates or projects. Completion of clinical trials by us or our licensees may take several years or more, but the length of time generally varies according to the type, complexity, novelty and intended use of a product candidate.

The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

- the number of sites included in the clinical trials;
- the length of time required to enroll suitable patients;
- the number of patients that participate in the clinical trials;
- the duration of patient follow-up;
- the development stage of the product candidate; and
- the efficacy and safety profile of the product candidate.

We expect our research and development expenses to increase in the future from current levels as we continue the advancement of our clinical trials and preclinical product development and to the extent we in-license new product candidates. The lengthy process of completing clinical trials and seeking regulatory approval for our product candidates requires expenditure of substantial resources. Any failure or delay in completing clinical trials, or in obtaining regulatory approvals, could cause a delay in generating product revenue and cause our research and development expenses to increase and, in turn, have a material adverse effect on our operations. Because of the factors set forth above, we are not able to estimate with any certainty when we would recognize any net cash inflows from our projects.

General and Administrative Expenses

General and administrative expenses consist primarily of compensation for employees in executive and operational functions, including accounting, finance, legal, business development, investor relations, information technology and human resources. Other significant general and administration costs include facilities costs, professional fees for outside accounting and legal services, travel costs, insurance premiums and depreciation.

Financial Expense and Income

Financial expense and income consists of interest earned on our cash and cash equivalents; bank fees and other transactional costs; expense or income resulting from fluctuations of the U.S. dollar and other currencies, in which a portion of our assets and liabilities are denominated, against the NIS (our functional currency); and fluctuations in the market value of our warrants which trade on the TASE.

Critical Accounting Policies and Estimates

Our accounting policies and their effect on our financial condition and results of operations are more fully described in our audited consolidated financial statements included elsewhere in this Annual Report. The preparation of financial statements in conformity with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, requires management to make estimates and assumptions that in certain circumstances affect the reported amounts of assets and liabilities, revenues and expenses and disclosure of contingent assets and liabilities. These estimates are prepared using our best judgment, after considering past and current events and economic conditions. While management believes the factors evaluated provide a meaningful basis for establishing and applying sound accounting policies, management cannot guarantee that the estimates will always be consistent with actual results. In addition, certain information relied upon by us in preparing such estimates includes internally generated financial and operating information, external market information, when available, and when necessary, information obtained from consultations with third party experts. Actual results could differ from these estimates and could have a material adverse effect on our reported results.

We believe that the accounting policies discussed below are critical to our financial results and to the understanding of our past and future performance, as these policies relate to the more significant areas involving management's estimates and assumptions. We consider an accounting estimate to be critical if: (1) it requires us to make assumptions because information was not available at the time or it included matters that were highly uncertain at the time we were making our estimate; and (2) changes in the estimate could have a material impact on our financial condition or results of operations.

Functional Currency

The presentation currency of our financial statements and our functional currency is the NIS. The functional currency of an entity in which we own an equity interest, which is referred to as oursubsidiary, differs from our functional currency, that subsidiary represents a foreign operation whose financial statements are translated as follows: (i) assets and liabilities are translated at the closing rate at the date of that balance sheet, (ii) income and expenses are translated at average exchange rates for the presented periods and (iii) share capital and capital reserves are translated at the exchange rate prevailing at the date of incurrence. All resulting translation differences are recognized in a separate component in equity, as other comprehensive loss, "adjustments from translation of financial statements."

For the convenience of the reader, the reported NIS amounts as of December 31, 2014 have been translated into U.S. dollars at the representative rate of exchange on December 31, 2014(U.S. $1 = NIS 3.889). The U.S. dollar amounts presented should not be construed as representing amounts that are receivable or payable in U.S. dollars or convertible into U.S. dollars, unless otherwise indicated. The U.S. dollar amounts were rounded to whole numbers of convenience.

Principles of Consolidation

Our financial statements reflect the consolidation of the financial statements of companies that we control based on legal control or effective control. We fully consolidate into our financial statements the results of operations of companies that we control. Legal control exists when we have the power, directly or indirectly, to govern the financial and operating policies of an entity. The effect of potential voting rights that are exercisable at the balance sheet date are considered when assessing whether we have legal control. In addition, we consolidate on the basis of effective control even if we do not have voting control. The determination that effective control exists involves significant judgment.

In evaluating the effective control on our investees we consider the following criteria to determine if effective control exists:

- whether we hold a significant voting interest (but less than half the voting rights);
- whether there is a wide diversity of public holdings of the remaining shares conferring voting rights;

- whether in the past we had the majority of the voting power participating in the general meetings of shareholders and, therefore, have in fact had the right to nominate the majority of the board members;
- the absence of a single entity that holds a significant portion of the investee's shares;
- our ability to establish policies and guide operations by appointing the remainder of the investee's senior management; and
- whether the minority shareholders have participation rights or other preferential rights, excluding traditional shareholder protective rights.

Entities we control are fully consolidated in our financial statements. All significant intercompany balances and transactions are eliminated in consolidation. Non-controlling interests of subsidiaries represent the non-controlling shareholders' proportionate interest in the comprehensive income (loss) of the subsidiaries and fair value of the net assets or the net identifiable assets upon the acquisition of the subsidiaries.

Revenue Recognition

We recognize revenues in accordance with International Accounting Standard No. 18, or IAS 18. Under IAS 18 we generate income from licensing agreements with pharmaceutical companies. These agreements usually comprise license fees, annual license fees, milestone payments and potential royalty payments.

Revenues are recognized in profit or loss when the revenues can be measured reliably, it is probable that the economic benefits associated with the transaction will flow to us and the costs incurred or to be incurred in respect of the transaction can be reliably measured.

Arrangements with multiple elements:

Revenues from sale agreements that do not contain a general right of return and that are composed of multiple elements such as licenses and services are allocated to the various accounting units and recognized for each accounting unit separately. An element constitutes a separate accounting unit if and only if it has a separate value to the customer. Revenue from the various accounting units is recognized when the criteria for revenue recognition regarding the elements of that accounting unit have been met according to their type and only to the extent of the consideration that is not contingent upon completion or performance of the remaining elements in the contract.

Revenues from license fees:

As for revenues from preliminary license fees and annual license fees, we examine whether the license can be separated from our other performance obligations.

Revenues from milestone payments:

Revenues which are contingent on compliance with and attainment of milestones are recognized in profit or loss at the achievement of a milestone, provided that certain criteria have been met.

Revenues from royalties:

Revenues from royalties are recognized as they accrue in accordance with the terms of the relevant agreement.

Share-based Compensation

We account for share-based compensation arrangements in accordance with the provisions of IFRS 2. IFRS 2 requires companies to recognize share-based compensation expense for awards of equity instruments based on the grant-date fair value of those awards. The cost is recognized as compensation expense over the vesting period, based upon the grant-date fair value of the equity or liability instruments issued. We selected the binomial option pricing model as the most appropriate method for determining the estimated fair value of our share-based awards without market conditions. The determination of the grant date fair value of options using an option pricing model is affected by estimates and assumptions regarding a number of complex and subjective variables. These variables include the expected volatility of our share price over the expected term of the options, share option exercise and forfeiture rate, risk-free interest rates, expected dividends and the price of our ordinary shares on the TASE. As our ordinary shares are publicly traded on the TASE, we do not need to estimate the fair value of our ordinary shares. Rather, we use the actual closing market price of our ordinary shares on the date of grant, as reported by the TASE although in the future may use the closing market price of our ADSs on the date of grant, as reported by the NYSE MKT..

If any of the assumptions used in the binomial option pricing model change significantly, share-based compensation for future awards may differ materially compared with the awards previously granted.

As for other service providers, the cost of the transactions is measured at the fair value of the goods or services received as consideration for equity instruments. In cases where the fair value of the goods or services received as consideration of equity instruments cannot be measured, they are measured by reference to the fair value of the equity instruments granted.

The cost of equity-settled transactions is recognized in profit or loss, together with a corresponding increase in equity, during the period which the service are to be satisfied, ending on the date on which the relevant employees or other service providers become fully entitled to the award.

If we modify the conditions on which equity-instruments are granted, an additional expense is recognized for any modification that increases the total fair value of the share-based payment arrangement or is otherwise beneficial to the employee or other service provider at the modification date.

Recently Issued Accounting Pronouncements

IFRS 9-Financial Instruments:

In July 2014, the IASB issued the final version of IFRS 9 Financial Instruments which reflects all phases of the financial instruments project and replaces IAS 39 Financial Instruments: Recognition and Measurement and all previous versions of IFRS 9. The standard introduces new requirements for classification and measurement, impairment, and hedge accounting. IFRS 9 is effective for annual periods beginning on or after 1 January 2018, with early application permitted. The adoption of IFRS 9 will have no material effect on the Company's financial assets on the financial statements.

US Registered Direct Offering

On December 8, 2014, we sold to certain institutional investors an aggregate of 1,797,753 ADSs in an at-the-market registered direct offering at $4.45 per share resulting in gross proceeds of $8,000,000. In addition, we issued to the investors unregistered warrants to purchase 898,877 ADSs. The warrants may be exercised at any time for a period of five years from issuance and have an exercise price of $4.45 per ADS, subject to adjustment as set forth therein. The warrants may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants. In connection with the private placement we paid an aggregate of $762,500 in placement agent fees and expenses and issued unregistered placement agent warrants to purchase 89,888 ADS, exercisable for five years from issuance, at an exercise price of $4.45 per ADS, subject to adjustment as set forth therein.

US Private Placement

On March 10, 2014, we sold to accredited investors 982,344 ADSs, at a purchase price of $5.15 per ADS, and warrants to purchase 491,172 additional ADSs in a private placement resulting in gross proceeds of $5,059,072. The warrants may be exercised at any time after September 10, 2014 for a period of four years from the date of issuance and have an exercise price of $6.43 per ADS, subject to adjustment as set forth therein. The warrants may be exercised on a cashless basis if after September 10, 2014 there is no effective registration statement registering the ADSs underlying the warrants. In connection with the private placement we paid an aggregate of $509,840 in placement agent fees and expenses and we issued placement agent warrants to purchase 49,117 ADSs exercisable at $6.43 per ADS for four years. The placement agent warrants may be exercised on a cashless basis at any time after September 10, 2014.

Israeli Public Offering

On February 5, 2013, we completed the sale in Israel of 7,477 units, each consisting of 10,000 of our ordinary shares, 5,000 Series 10 Warrants to purchase ordinary shares and 5,000 Series 11 Warrants to purchase ordinary shares, for an aggregate of 74,770,000 ordinary shares, 50,000,000 Series 10 Warrants to purchase ordinary shares and 50,000,000 Series 11 Warrants to purchase ordinary shares. The purchase price in the offering was NIS 3,544 per unit ($960.17 based on the exchange rate of New Israel Shekels to U.S. Dollars of NIS 3.691 to $1.00), for an aggregate purchase price for all units of NIS 26,498,488 ($7,179,216.47 using the same exchange rate). After the payment of sales commissions, we received net proceeds from the offering of NIS 23,926,000 ($6,402,000).

On October 23, 2013, we completed the sale in Israel of 3,675 units, each consisting of 500 of our ordinary shares and 375 Series 12 Warrants to purchase ordinary shares, for an aggregate of 1,837,500 ordinary shares and 1,378,125 Series 12 Warrants to purchase ordinary shares. The purchase price in the offering was NIS 5,800 per unit ($1,648 based on the exchange rate of New Israel Shekels to U.S. Dollars of NIS 3.52 to $1.00), for an aggregate purchase price for all units of NIS 21,315,000 ($6,055,398 using the same exchange rate). After the payment of sales commissions, we received net proceeds from the offering of NIS 20,138,000 ($5,721,000).

Israeli Public Warrant Offerings

Series 6 and 7 Warrants

In connection with our Israeli public offering on November 16, 2011, we issued Series 6 and Series 7 Warrants, which were publicly traded on the TASE and exercisable into our publicly traded ordinary shares. In accordance with IFRS, we allocated a portion of the consideration received for such warrants based on their market value at that time. The consideration allocated to such warrants is generally reflected in non-current liabilities due to the fact that the exercise price of the warrants is linked to the Israeli consumer price index.

In the public offering, we issued 4,953,750 Series 6 Warrants exercisable for 198,150 of our ordinary shares. The Series 6 Warrants have an exercise price of 15.75 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and were originally scheduled to expire on May 16, 2012. On August 18, 2012,we filed an application with the Petah-Tikva District Court in Israel to approve an extension of the Series 6 Warrants until September 1, 2014 and following a meeting of our shareholders and holders of Series 6 Warrant to approve the extension of the exercise period of the Series 6 Warrants, on January 27, 2014, the District Court approved the extension until October 30, 2013. The Series 6 Warrants expired on October 30, 2013.

In the same offering, we issued 9,907,500 Series 7 Warrants exercisable for 396,300 of our ordinary shares. The Series 7 Warrants have an exercise price of 20 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and were originally scheduled to expire on November 16, 2013. On November 7, 2013,we filed an application with the Petah-Tikva District Court in Israel to approve an extension of the Series 7 Warrants until March 31, 2014 and following a meeting of our shareholders and holders of Series 7 Warrant to approve the extension of the exercise period of the Series 7 Warrants, on January 27, 2014, the District Court approved the extension until March 31, 2014. The series 7 warrants expired on March 31, 2014.

Series 8 and 9 Warrants

In connection with our Israeli public offering on May 1, 2012, we issued Series 8 and Series 9 Warrants, which are publicly traded on the TASE and exercisable into our publicly traded ordinary shares. In accordance with IFRS, we allocated a portion of the consideration received for such warrants based on their market value at the time. The consideration allocated to warrants is generally reflected in non-current liabilities due to the fact that the exercise price of such warrants is linked to the Israeli consumer price index.

We issued 8,112,000 Series 8 Warrants exercisable for 324,480 of our ordinary shares in the offering. Although the Series 8 Warrants had an exercise price of 13.75 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and were set to expire on June 30, 2013. On June 24, 2013, the Lod District Court in Israel approved a settlement, approved at a meeting of the shareholders and the Series 8 Warrants holders, according to which the exercise price was increased to 18.75 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and the exercise period was extended until December 31, 2013.The Series 8 Warrants expired on December 31, 2013.

We also issued 12,168,000 Series 9 Warrants exercisable for 486,720 of our ordinary shares in this offering. In accordance with IFRS, we allocated a portion of the consideration received from the Series 9 Warrants based on their market value at the time. The consideration allocated to the Series 9 Warrants is generally reflected in shareholders' equity due to the fact that the exercise price of such warrants is fixed. The Series 9 Warrants have a fixed exercise price of 21.25 NIS per ordinary share and are set to expire on May 1, 2015.

Series 10 and 11 Warrants

In connection with our Israeli public offering on February 5, 2013, we issued Series 10 and Series 11 Warrants, which are publicly traded on the TASE and exercisable into our publicly traded ordinary shares. In accordance with IFRS, we allocated a portion of the consideration received for such warrants based on their market value at the time. The consideration allocated to warrants is generally reflected in non-current liabilities due to the fact that the exercise price of such warrants is linked to the Israeli consumer price index.

We issued 39,067,000 Series 10 Warrants exercisable for 1,562,680 of our ordinary shares in the offering. The Series 10 Warrants have an exercise price of 0.394 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and are set to expire on October 31, 2015.

We also issued 37,385,000 Series 11 Warrants exercisable for 1,495,400 of our ordinary shares in the offering. The Series 10 Warrants have an exercise price of 0.392 NIS per ordinary share (which may fluctuate as it is based on the Israeli consumer price index) and are set to expire on April 30, 2016.

Our Board of Directors decided that the exercise price of the Series 10 and Series 11 Warrants will no longer be linked to the Israeli consumer price index and on August 20, 2013, the Lod District Court approved a settlement, approved at a meeting of the shareholders and the Series 10 and 11Warrants holders, according to which the exercise price of the Series 10 and 11 Warrants will no longer be linked to the Israeli consumer price index. As a result, Series 10 and 11 Warrants, were reclassified to equity.

As of March 23, 2015, other than Series 6, Series 7 and Series 8 Warrants that have been expired, 25,000 Series 10 Warrants exercised on December 26, 2013 to purchase 1,000 ordinary shares for an aggregate exercise price of NIS 9,850 and 12,500 Series 11 Warrants exercised on December 26, 2013 to purchase 500 ordinary shares for an aggregate exercise price of NIS 4,900 none of the foregoing warrants have been exercised.

Jumpstart Our Business Startups Act of 2012

We are an emerging growth company within the meaning of the rules under the Securities Act, and we will utilize certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies. The JOBS Act permits us, as an "emerging growth company," to take advantage of an extended transition period to comply with certain new or revised accounting standards if such standards apply to companies that are not issuers. We are choosing to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by issuers. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

A. Results of Operations

Comparison of the Year Ended December 31, 2014 to Year Ended December 31, 2013

Research and development expenses

Research and development expenses for the year ended December 31, 2014 were NIS 16.20 million, an increase of NIS 0.81 million, or 5.3%, compared to NIS 15.39 million for the year ended December 31, 2013. The increase in research and development expenses was primarily due to the increase in clinical trial expenses. We expect that we will continue to experience increases in research and development expenses through 2015 and beyond.

General and administrative expenses

General and administrative expenses were NIS11.57 million for the year ended December 31, 2014 and NIS 15.92 million for year ended December 31, 2013. This decrease was primarily due to a decrease in investor relations expenses, share based payments, salaries and professional services. We expect that general and administrative expenses will remain at the same level through 2015 and beyond.

Financial income, net

We recognized net financial income of NIS 3.27 million for year ended December 31, 2014, and NIS 0.51 million for the year ended December 31, 2013. The increase in the financial income, net is mainly due to a decrease in the fair market value of the warrants exercisable into shares and also the increase in the exchange rate of the USD against the NIS.

Comparison of the Year Ended December 31, 2013 to Year Ended December 31, 2012

Research and development expenses

Research and development expenses for the year ended December 31, 2013 were NIS 15.39 million, an increase of NIS 2.23 million, or 16.9%, compared to NIS 13.16 million for the year ended December 31, 2012.

The increase in research and development expenses was primarily due to the increase in clinical trial expenses. We expect that we will continue to experience increases in research and development expenses through 2015 and beyond.

General and administrative expenses

General and administrative expenses were NIS 15.92 million for the year ended December 31, 2013 and NIS 9.3 million for year ended December 31, 2012. The increase in 2013 as compared to 2012 was in investor relations expenses, share based payments, salaries and professional services.

Financial income, net

We recognized net financial income of NIS 0.509 million for year ended December 31, 2013, a decrease of NIS 0.005 million, or 9.7%, compared to net financial income of NIS 0.514 million for the year ended December 31, 2012. The decrease in net financial income, net is not material.

B. Liquidity and Capital Resources

Since inception, we have funded our operations primarily through public (in Israel) and private offerings of our equity securities and payments received under our strategic licensing arrangements. At December 31, 2014, we had approximately NIS 36.1 million in cash and cash equivalents, and have invested most of our available cash funds in short-term bank deposits. As of March 23, 2015, we raised approximately NIS 92 million, after deduction of offering expenses, as a private company until the consummation of the IPO and approximately NIS 193 million, after deduction of offering expenses, as a public company since the completion of the IPO. During 2014, we raised an aggregate of NIS 45 million, from a private placement and registered direct offering conducted in the US.

We may be able to use U.S. taxes withheld as credits against Israeli corporate income tax when we have income, if at all, but there can be no assurance that we will be able to realize the credits. In addition, we believe that we may be entitled to a refund of such withholding tax from the U.S. government but there can be no assurance that we will be entitled to such a refund. For information regarding the revenues and expenses associated with our licensing agreements, see "Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements", "Item 4. Information on the Company—Business Overview—In-Licensing Agreements" and "Item 5. Operating and Financial Review and Prospects—Revenues."

Net cash used in operating activities was NIS 28.6 million for the year ended December 31, 2014, compared with net cash used in operating activities of NIS 30.1 million and NIS 16.2 million for the years ended December 31, 2013 and 2012, respectively. The NIS 1.5 million decrease in the net cash used in operating activities during 2014, compared to 2013, was primarily the result of a decrease in the loss of the company and also the result of an increase in accounts receivable and decrease in trade payables and other payable, which increased in the year before. The NIS 13.9 million increase in the net cash used in operating activities during 2013, compared to 2012, was primarily the result of an increase in the loss of the company and also the result of decrease in trade payables and an increase in other payable and accounts receivable, which decreased in the year before.

Net cash used in investing activities for the year ended December 31, 2014 was NIS 0.04 million compared to net cash used in investing activities of NIS 0.04 million for the year ended December 31, 2013 and net cash provided by investing activities of NIS 0.07 million for the year ended December 31, 2012. The changes in cash flows from investing activities are immaterial.

Net cash provided by financing activities was NIS 44.7 million for the year ended December 31, 2014, compared to net cash provided by financing activities of NIS 46 million for the year ended December 31, 2013 and NIS 5.6 million for the year ended December 31, 2012. The NIS 1.3 million decrease in the net cash provided by financing activities during 2014, compared to 2013, was primarily due to sale of treasury shares in 2013. The NIS 40.4 million increase in the net cash provided by financing activities during 2013, compared to 2012, was primarily due to our capital raising transactions in February and October 2013.

Developing drugs, conducting clinical trials and commercializing products is expensive and we will need to raise substantial additional funds to achieve our strategic objectives. Although we believe our existing financial resources as of March 232015, will be sufficient to fund our projected cash requirements through for the next twelve months, we will require significant additional financing to fund our operations. Additional financing may not be available on acceptable terms, if at all. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- the amount of revenues we receive under our licensing arrangements;
- the costs of the development and expansion of our operational infrastructure;
- the costs and timing of obtaining regulatory approval of our platform and products;
- the ability of us or our collaborators to achieve development milestones, marketing approval and other events or developments under our licensing agreements;
- the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs and timing of securing manufacturing arrangements for clinical or commercial production;

- the costs of contracting with third parties to provide sales and marketing capabilities for us;
- the costs of acquiring or undertaking development and commercialization efforts for any future products or platforms;
- the magnitude of our general and administrative expenses;
- any cost that we may incur under current and future licensing arrangements relating to our platform and products; and

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through payments received under our license agreements, debt or equity financings, or by out-licensing other product candidates. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts.

C. Research and Development, Patents and Licenses, Etc.

For information concerning our research and development policies and a description of the amount spent during each of the last three fiscal years on company-sponsored research and development activities, see "Item 5. Operating and Financial Review and Prospects—Operating Results."

D. Trend Information.

We are a development stage company and it is not possible for us to predict with any degree of accuracy the outcome of our research, development or commercialization efforts. As such, it is not possible for us to predict with any degree of accuracy any significant trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on our net sales or revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause financial information to not necessarily be indicative of future operating results or financial condition. However, to the extent possible, certain trends, uncertainties, demands, commitments and events are identified in the preceding subsections of this Item 5.

E. Off-Balance Sheet Arrangements.

We have no off-balance sheet arrangements that have had or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that are material to investors.

F. Contractual Obligations.

The following table summarizes our significant contractual obligations in NIS at December 31, 2014:

Contractual Obligations	Total	Less than 1 year	1 – 3 years	3-5 years	More than 5 years
NIH milestones[1]	1,652,825	1,652,825	-	-	-
Leiden University milestones[2]	377,968	47,246	330,722	-	-
Car lease obligations	212,000	144,000	68,000	-	-
Severance pay	224,000	-	-	-	224,000
Total	2,466,793	1,844,071	398,722		224,000

(1) Includes $425,000 in milestone payments. Does not include a potential milestone payment of $500,000 upon approval by the FDA or any regulatory authority as the NIH Agreement will terminate in 2015 upon the expiration of the last patent licensed thereunder, which will be prior to achieving such milestone.

(2) Includes a €10,000 annual royalty and €50,000 upon the initiation of a Phase I study. We will update our milestone payment obligations upon releasing the Phase I data from such study. As such, the obligations above do not include a potential milestone payment of €100,000 upon the initiation of a Phase II study, €200,000 upon the initiation of a Phase III study or €500,000 upon marketing approval by any regulatory authority.

ITEM 6. Directors, Senior Management and Employees

A. Directors and Senior Management.

The following table sets forth the members of our senior management and Board of Directors:

Member	Position	Age
Ilan Cohn, Ph.D.	Chairman of the Board	59
Pnina Fishman, Ph.D.	Chief Executive Officer, Director	66
Motti Farbstein	Chief Operating and Financial Officer	51
Guy Regev	Director	47
Abraham Sartani, M.D.	Director	68
Gil Oren	Director, Audit Committee and Compensation Committee member	62
Israel Shamay	Director, Audit Committee and Compensation Committee member	51

Ilan Cohn, Ph.D. Ilan Cohn, Ph.D. is a patent attorney and senior partner at the patent attorney firm Reinhold Cohn and Partners, where he has been an attorney since 1986. Dr. Cohn co-founded Can-Fite, served as its Chief Executive Officer until September 2004, served on our Board of Directors since 1994 and since May 30, 2013 servesas the Chairman of the Can-Fite Board of Directors. Dr. Cohn has also been a director of OphthaliX since November 21, 2011. Dr. Cohn holds a Ph.D. in biology and is a patent attorney with many years of experience in the biopharmaceutical field. He has served on the Board of Directors of a number of life science companies, including Discovery Laboratories Inc. (formerly Ansan Pharmaceuticals), a U.S. public company. Dr. Cohn has also been involved in the past in management of venture capital funds focused on investments in the life sciences industry. Dr. Cohn served a number of years as a co-chairman of the Biotech Committee of the US-Israeli Science and Technology Commission. Dr. Cohen is also currently a member of the Board of Directors of I.C.R.C Management Ltd, Famillion BVI Ltd. and Famillion Ltd. (a subsidiary of Famillion BVI Ltd.). Dr. Cohn holds a Ph.D. in Biology from the Hebrew University of Jerusalem.

Pnina Fishman, Ph.D. Pnina Fishman, Ph.D. co-founded Can-Fite and has served as our Chief Executive Officer and served on our Board of Directors since September 2005. She has also served as the Chief Executive Officer of OphthaliX from November 21, 2011 through December 31, 2012. Dr. Fishman is the scientific founder of Can-Fite and was previously a professor of Life Sciences and headed the Laboratory of Clinical and Tumor Immunology at the Felsenstein Medical Research Institute, Rabin Medical Center, Israel. Dr. Fishman has authored or co-authored over 150 publications and presented the findings of her research at many major scientific meetings. Her past managerial experience included seven years as Chief Executive Officer of Mor Research Application, the technology transfer arm of Clalit Health Services, the largest healthcare provider in Israel. Mor Research Application was also the first clinical research organization in Israel. Dr. Fishman currently also serves as a member of the Board of Directors of F.D Consulting Ltd., Ultratrend Ltd., EyeFite Ltd. and OphthaliX Inc. Dr. Fishman holds a Ph.D. in Immunology from the Bar Ilan University in Ramat Gan, Israel.

Motti Farbstein. Motti Farbstein has been with Can-Fite since 2003. Mr. Farbstein served as our Chief Operating Officer from August 2003 until May 2005 and from that date onwards he served as Chief Operating and Financial Officer. Mr. Farbstein also serves as a director of EyeFite Ltd. since July 2011. Mr. Farbstein's past managerial experience includes seven years as Vice President of Mor Research Application, a company that managed the commercialization of the intellectual property of all hospitals and research centers affiliated with Clalit Health Services, which is the largest healthcare provider in Israel and was Israel's first clinical CRO. Mr. Farbstein also has extensive experience in the data management of clinical trials.

Guy Regev. Guy Regev has over twelve years of experience in accounting, financial management and control and general management of commercial enterprises. He has served on our Board of Directors since July 2011 and has served as a member of our Audit Committee and Compensation Committee since February 2014. Mr. Regev has also been a director of OphthaliX since November 2011. Mr. Regev is currently the Chief Executive Officer of Gaon Holdings Ltd, a publicly traded Israeli holding company traded on the TASE which focuses on three areas of operation - Cleantech / Water, Financial Services, Retail/Trading. Mr. Regev is currently also the Chief Executive Officer of Middle East Tube Company Ltd a publicly traded Israeli company traded on the TASE which focuses on steel pipe manufacturing and galvanization services. Mr. Regev was the Chief Executive Officer of Shaked Global Group Ltd, a privately-held equity investment firm that provides value added capital to environmental-related companies and technologies. Prior to joining Shaked, from 2001 to 2008, Mr. Regev was Vice President of Commercial Business at Housing & Construction Holding, or HCH, Israel's largest infrastructure company. His duties included being responsible for the consolidation and financial recovery of various business units within HCH. Prior to that, Mr. Regev carried several roles within the group including as a Chief Financial Officer and later the Chief Executive Officer of Blue-Green Ltd., the environmental services subsidiary of HCH. Between 1999 and 2001, Mr. Regev was a manager at Deloitte & Touche, Israel. Mr. Regev holds an LLB degree in Law (Israel) and is a licensed attorney and has been a licensed CPA since 1999. Mr. Regev is also a director of, The Green Way Ltd, Shtang Construction and Engineering Ltd, R.I.B.E. Consulting & Investment Ltd., Middle East Tube Company Ltd, Middle East Tube - Industries 2001 Ltd, Middle East Tubes - Galvanizing (1994) Ltd, I-Solar Greentech Ltd, Plassim Infrastructure Ltd, Plassim Advanced Solutions in Sanitation Ltd, Hakohav Valves Industries Metal (1987) Ltd, Metzerplas Agriculture Cooperative Ltd, B. Gaon Retail & Trading Ltd, Gaon Agro - Rimon Management Services Ltd, B. Gaon Business (2004) Ltd, Gaon Antan Investments Ltd, Or Asaf Investments Ltd, Hamashbir Holdings (1999) Ltd, and AHAVA Holdings LTD.

Abraham Sartani, M.D. Abraham Sartani has served on our Board of Directors since 2001. Dr. Sartani has over 30 years of experience in the pharmaceuticals industry and currently acts as a consultant to pharmaceutical and medical device companies. Dr. Sartani is a member of a number of scientific and management societies and the author or co-author of numerous publications and patents in the urology, pain treatment and hypertension fields. Dr. Sartani also currently serves on the Board of Directors of Akkadeas Pharma Srl and is a co-founding partner. From 1985 until 2008, Dr. Sartani was the Vice-President of R&D and Licensing of Recordati, a European specialty pharmaceutical company. Prior to joining Recordati, from 1980 until 1985, Dr. Sartani was employed at Farmitalia-Carlo Erba, serving in a number of capacities, including as the Medical Director for Europe.

Gil Oren. Gil Oren has served as external director on our Board of Directors since July 2008 and chairs both the Audit Committee and Compensation Committee since July 2008. Mr. Oren is the founder of a private consulting firm he started in 2008. Mr. Oren has over 25 years of experience in top managerial positions in various public companies in Israel and the United States and currently serves on the Board of Directors of Pointer Telocation Ltd. (NASDAQ: PNTR). From 1976 to 1992, Mr. Oren served in various positions within the Tadiran Group, including serving for five years as the Chief Financial Officer of Tadiran Electronic's U.S. subsidiary. After serving in such capacity, Mr. Oren returned to Israel and joined Cargal, first as Vice President of Finance and then as Chief Executive Officer and General Manager. From 2002 to 2007, Mr. Oren joined SFK, a leading Israeli investment group, and served in various capacities in its portfolio companies, including as the deputy chief executive office of Urdan Industries, the chief executive officer of Itong Industries and the chairman of the Board of Directors of Orlite Industries. Mr. Oren has also served, on behalf of SFK, on the Board of Directors of various other public and private companies, including Nirlat, Aloni and Scope. Mr. Oren holds a B.A in accounting and economics from Tel Aviv University and a M.B.A from Tel Aviv University. Mr. Oren is also Certified Public Accountant.

Israel Shamay has served as external director on our Board of Directors since December 2014 and serves as a member on both the Audit Committee and Compensation Committee. Since 2012 Mr. Shamay has served as Executive Director, Strategic Initiatives and Head of the Americas Operations of MATIMOP (Israeli Industry Center for R&D), the International Operations agency of the Israeli Office of the Chief Scientist, focusing on developing and implementing cooperation platforms for industrial R&D and innovation projects in the Americas region. From 2006 until 2012 Mr. Shamay served as Executive Director of European Cooperations at MATIMOP, where he was in charge of architecting, realizing and evaluating industrial innovation cooperation frameworks at bilateral and European level, making them a major R&D cooperation instrument for Israeli industry with Europe. Between 2010 and 2011, Mr. Shamay was Head of the Israeli EUREKA Chairmanship Program (EUREKA is Europe's largest innovation network with nearly 40 member states). The Israeli EUREKA Chairmanship focused on developing new financial instruments for innovative small and medium sized enterprises and on expanding EUREKA's international dimension. From 2002 Mr. Shamay served as Israel's National Representative in several international R&D programs, from 2005 as an expert evaluator for the EU Framework Programs for R&D and from 2006 until 2009 managed the Israeli R&D collaboration with the EU Global Satellite Navigation Program – GALILEO. From 1991 till 2001 Mr. Shamay served in senior technical, marketing and executive positions in Israeli hi-tech companies operating globally, including the RAD group and Comverse Technologies. Mr. Shamay is an MBA graduate of the Recanati School of Business at the Tel-Aviv University and a graduate of the Technion in Haifa, faculty of Information Systems Engineering.

B. Compensation.

Compensation of Senior Management and Directors

The following table presents in the aggregate all compensation we paid to all of our senior management and directors as a group for the year ended December 31, 2014. This amount does not include business travel, professional and business association dues and expenses reimbursed to executive officers, and other benefits commonly reimbursed or paid by companies in Israel.

	Salaries, fees, commissions and bonuses and options (NIS in Thousands)
All senior management and directors as a group, consisting of 7 persons	3,148

The following table sets forth information with respect to the options granted to the members of our senior management and Board of Directors for the year ended December 31, 2014.

Name	Date of Grant	Purchase Price	Number of Options	Vesting Period	Expiration Date	Total Benefit (in NIS)	Benefit recognized in 2014 (in NIS)
Gil Oren	July 14, 2014	12	10,000	1/36 per month	July 14, 2017	15,662	2,752

Although as a public company with shares listed only on the TASE and NYSE MKT, we are exempt from complying with the requirements of the Israeli law that require the disclosure of the compensation, on an individual basis, of a company's five most highly compensated senior executive officers, we have elected to provide such information in our annual reports. Accordingly, the following table presents information regarding compensation accrued in our financial statements for our five most highly compensated senior executive officers, namely our Chief Executive Officer, Chief Financial Officer, Vice President, Operations, Vice President, Clinical Development & IP and Vice President, Research and Development, as of December 31, 2014.

Name and Position	Salary	Bonus(1)	Value of Options Granted(2)	Other(3)	Total
	(NIS in thousands)				
Pnina Fishman *Chief Executive Officer*	1,050	262	0	57	1,369
Motti Farbstein *Chief Financial Officer*	814	148	8	53	1,023
Barak Singer (4) *Former* Vice-President of Business Development	483	0	(178)	34	339
Gil Oren *Director*	122	-	3	-	125
Guy Regev *Director*	116	-	5	-	121

(1) The annual bonus is subject to the fulfillment of certain targets determined for each year by the board of directors (for our Chief Executive Officer) and by our Chief Executive Officer (for our other executive officers).

(2) The value of options is the expense recorded in our financial statements for the period ended December 31, 2014 with respect to all options granted to such executive officer.

(3) Cost of use of company car.

(4) Barak Singer ceased serving as Vice President of Business Development on July 28, 2014.

Employment and Consulting Agreements

We have or have had written employment and non-competition agreements with each of Barak Singer, our former Vice President of Business Development, Motti Farbstein, our Chief Operating and Financial Officer, Sari Furman, our Director of Clinical Operations and written consulting agreements with each of Reinhold Cohn and Partners, an Israeli partnership, through which Ilan Cohn, Ph.D., our Chairman of the Board of Directors, is a partner, Abraham Sartani, one of our directors, and BioStrategies Consulting Ltd., a U.S. company, or BioStrategics, through its President Michael Silverman, our Medical Director. We have also entered into a service management agreement with F.D. Consulting International and Marketing Ltd., an Israeli limited company, or F.D. Consulting, which is partially owned by Pnina Fishman, Ph.D., our Chief Executive Officer and director, and master services agreement with Accellient Partners LLC, a Massachusetts limited liability company, or Accellient Partners, through its Chief Executive Officer William Kerns, our Vice President of Drug Development. As of March 23, 2015, the foregoing agreements were still in full force and effect, with the exception of (i) the consulting agreement with Reinhold Cohn and Partners, which expired by its terms in September 2011 and was not subsequently extended, (ii) the consulting agreement with Abraham Sartani, which we terminated in July 2011, (iii) the consulting agreement with Avigdor Kaplan, which was terminated in May 2013, and (iv) the employment agreement with Barak Singer.

All of these agreements contain customary provisions regarding noncompetition, confidentiality of information and assignment of proprietary information and inventions. However, the enforceability of the noncompetition provisions may be limited under applicable law. The compensation payable under the foregoing agreements consists of share-based awards and/or an hourly rate for services rendered, reimbursement of certain expenses, and in the case of the employment and non-competition agreements, contributions to study funds.

The following are summary descriptions of each of the foregoing agreements which are still in force to which we are a party. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this Annual Report on Form 20-F.

Employment and Non-Competition Agreement with Motti Farbstein: On September 1, 2003 we entered into an employment and non-competition agreement with Motti Farbstein pursuant to which Mr. Farbstein began serving as our Director of Clinical Operations and Administrative Affairs on September 1, 2003 and is currently serving as our Chief Operating and Financial Officer. Mr. Farbstein's current gross monthly salary is NIS 49,450. Mr. Farbstein is entitled to an allocation to a manager's insurance policy equivalent to an amount up to 13-1/3% of his gross monthly salary, up to 2-1/2% of his gross monthly salary for disability insurance and 7-1/2% of his gross monthly salary for a study fund. The foregoing amounts are paid by us. Five percent of his gross monthly salary is deducted for the manager's insurance policy and 2-1/2% is deducted for the study fund. Mr. Farbstein is also entitled to reimbursement for reasonable out-of-pocket expenses, including travel expenses, and use of a company automobile and mobile phone.

Mr. Farbstein is also entitled to receive options exercisable into our ordinary shares from time to time. As of March 23, 2015, we have granted him options to purchase 54,196ordinary shares, of which 1,133 were exercised into shares.

The term of Mr. Farbstein's employment and non-competition agreement is indefinite, unless earlier terminated for just cause by either party, upon the death, disability or retirement age, or without cause by either party, subject to 60 days' advanced notice.

Employment and Non-Competition Agreement with Barak Singer: On February 22, 2011 we entered into an employment and non-competition agreement which was subsequently amended on February 28, 2013. Barak Singer began serving as our Vice President of Business Development on March 20, 2011 and was appointed Chief Executive Officer of Ophthalix on February 28, 2013. Mr. Singer's current gross monthly salary is NIS 45,000 (50% of this amount is consideration for services provided to our company and 50% is for services provided to OphthaliX). Mr. Singer was entitled to a success performance bonus of one time his monthly salary upon the achievement of certain milestones. In addition, he was issued options to purchase 104,412 shares of OphthaliX's common stock of vesting over three years on a quarterly basis and exercisable at $5.29 per share options as well as options purchase 104,412 shares of OphthaliX's common stock exercisable at $5.29 and vesting on the achievement of certain milestones. Mr. Singer was entitled to an allocation to a manager's insurance policy equivalent to an amount up to 13-1/3% of his gross monthly salary, up to 2-1/2% of his gross monthly salary for disability insurance and 7-1/2% of his gross monthly salary for a study fund. The foregoing amounts were paid by us. Five percent of his gross monthly salary was deducted for the manager's insurance policy and 2-1/2% is deducted for the study fund. Mr. Singer was also entitled to reimbursement for reasonable out-of-pocket expenses and use of a company automobile and mobile phone. Mr. Singer was also entitled to receive options exercisable into our ordinary shares from time to time. On July 28, 2014, Mr. Singer ceased his employment with us. As of the date of termination, he had outstanding options to purchase 17,200 ordinary shares and all options were forfeited on October 28, 2014.

The term of Mr. Singer's employment is indefinite, unless earlier terminated for just cause by either party, upon the death, disability or retirement age, or without cause by either party, subject to 60 days' advanced notice.

Consulting Agreement with BioStrategics: On September 27, 2005, we entered into a consulting agreement with BioStrategics through its President, Michael Silverman pursuant to which Dr. Silverman began serving as our Medical Director. Dr. Silverman has extensive experience in clinical development acquired through his involvement in clinical development in large pharmaceutical and small biopharmaceutical companies. He was involved in international clinical research, market-oriented strategic planning, and the challenges of managing research and development portfolios in various capacities at Sterling Winthrop Research Institute and subsequently at Sandoz Research Institute.

BioStrategics' current fee is $325 per hour with a maximum daily fee of $2,600. In addition, BioStrategics is entitled to reimbursement for reasonable pre-approved expenses. The term of the consulting agreement is currently on a year-to-year basis, unless earlier terminated by either party upon 30 days' prior written notice or immediately by either party if such termination is for cause.

Service Management Agreement with F.D. Consulting: On June 27, 2002, we entered into a Service Management Agreement with F.D. Consulting, a company partially owned by Pnina Fishman, pursuant to which Dr. Fishman began serving as our Chief Scientific Officer and later became our Chief Executive Officer and is a member of our Board of Directors and continues to be retained through this agreement. F.D. Consulting's current gross monthly fee is NIS 75,000, which is linked to the Israeli CPI and fluctuates accordingly. Dr. Fishman, through F.D. Consulting, is also entitled to reimbursement for reasonable out-of-pocket expenses and use of a company automobile and mobile phone.

Dr. Fishman is also entitled to receive options exercisable into our ordinary shares from time to time. As of March 23, 2015, we have granted her options to purchase 544,442 ordinary shares, of which 241,612 were exercised into shares.

The term of F.D. Consulting's service management agreement is indefinite, unless earlier terminated for cause by us or without cause by either party, subject to three months' advanced notice.

Master Services Agreement with Accellient Partners: On May 10, 2010, we entered into a Master Services Agreement with Accellient Partners, a company owned by William Kerns, who currently serves as our current Vice President of Drug Development. Dr. Kerns has over 20 years of experience in Pharmaceutical Research and Development at SmithKline Beecham and Eisai Pharmaceuticals. As a Senior Executive he has participated in the development of drugs for over 100 Phase I studies and 13 NDA's and/or Marketing Authorization Applications. Dr. Kerns has chaired a FDA committee on biomarkers and he is an expert in preclinical development and regulatory strategy.

According to the agreement, consulting services are provided by Accellient Partners' personnel in accordance with individual work orders that are executed from time to time. Each individual work order defines the scope of work to be provided and sets forth the fees to be paid to Accellient Partners.

Beginning on May 10, 2012, the term of the master services agreement is on a month-to-month basis, unless terminated by us upon 30 days' prior written notice, by us at any time if Accellient Partners commits a breach and fails to cure, or by Accellient Partners upon 30 days' prior written notice if we commit a breach and fail to cure.

Reinhold Cohn and Partners: Reinhold Cohn and Partners, an Israeli partnership, of which Ilan Cohn, Ph.D. is a partner provides intellectual property legal services to us in the ordinary course of business.

C. Board Practices

General

According to the Israeli Companies Law, the management of our business is vested in our Board of Directors. Our Board of Directors may exercise all powers and may take all actions that are not specifically granted to our shareholders. Our executive officers are responsible for our day-to-day management and have individual responsibilities established by our Board of Directors. Executive officers are appointed by and serve at the discretion of our Board of Directors, subject to any applicable employment agreements we have entered into with the executive officers. See "Item 6—Directors, Senior Management and Employees—Compensation—Employment and Consulting Agreements."

Election of Directors and Terms of Office

Our Board of Directors currently consists of six members. Other than our two external directors, our directors are elected by an ordinary resolution at the annual general meeting of our shareholders. The nomination of our directors is proposed by the Board of Directors. Our board has the authority to add additional directors up to the maximum number of 12 directors allowed under our Articles. Such directors appointed by the board serve until the next annual general meeting of the shareholders. Unless they resign before the end of their term or are removed in accordance with our Articles of Association, all of our directors, other than our external directors, will serve as directors until our next annual general meeting of shareholders. On July 14, 2014, at an annual general meeting of our shareholders, Pnina Fishman, Ilan Cohn, Liora Lev, Avi Sartani, and Guy Regev were re-elected to serve as directors for a term expiring at our next annual general meeting of shareholders and until his or her respective successor is duly elected. At the same meeting, Gil Oren was re-elected to serve as one of our external directors for an additional three-year term ending July 9, 2017. On December 31, 2014, at a special meeting of our shareholders, Israel Shamay was elected to serve for a three-year term ending December 30, 2017 as one of our external directors, replacing Yechezkel Barenholtz who served the maximum term according to the provisions of Israeli Companies Law. Israel Shamay may be re-elected for another two three-year terms. Gil Oren may not be re-elected to serve as an external director as he was elected for three terms, the maximum term according to the provisions of the Israeli Companies Law. On May 30, 2013, Ilan Cohn was appointed as Chairman of the Board and on January, 2014, Liora Lev resigned from the Board of Directors.

None of our directors or officers has any family relationship with any other director or officer. None of our directors have service contracts that provide for benefits upon termination of his or her directorship with us, other than the payment of salary due, accrued and unpaid as of and through the date of termination. See "Item 6—Directors, Senior Management and Employees—Compensation—Employment and Consulting Agreements."

Chairman of the Board. Under the Israeli Companies Law, without shareholder approval, a person cannot hold the role of both chairman of the board of directors and chief executive officer of a company. Furthermore, a person who is directly or indirectly subordinate to a chief executive officer of a company may not serve as the chairman of the board of directors of that company and the chairman of the board of directors may not otherwise serve in any other capacity in a company or in a subsidiary of that company other than as the chairman of the board of directors of such a subsidiary.

The Israeli Companies Law provides that an Israeli company may, under certain circumstances, exculpate an office holder from liability with respect to a breach of his duty of care toward the company if appropriate provisions allowing such exculpation are included in its articles of association. Our Articles of Association permit us to maintain directors' and officers' liability insurance and to indemnify our directors and officers for actions performed on behalf of us, subject to specified limitations. We maintain a directors and officers insurance policy which covers the liability of our directors and officers as allowed under the Israeli Companies Law.

The term office holder is defined in the Israeli Companies Law as a director, general manager, chief business manager, deputy general manager, vice general manager, executive vice president, vice president, any other manager directly subordinate to the general manager or any other person assuming the responsibilities of any of the foregoing positions, without regard to such person's title. Each person listed above in "Item 6—Directors, Senior Management and Employees—Directors and Senior Management" is an office holder, as defined in the Israeli Companies Law.

External and Independent Directors

Under the Israeli Companies Law, the boards of directors of companies whose shares are publicly traded, either within or outside of Israel, are required to include at least two members who qualify as external directors.

External directors must be elected by a majority vote of the shares present and voting at a shareholders meeting, provided that either:

- the majority of the shares that are voted at the meeting, including at least a majority of the shares held by non-controlling shareholders who do not have a personal interest in the election of the external director (other than a personal interest not deriving from a relationship with a controlling shareholder) who voted at the meeting, excluding abstentions, vote in favor of the election of the external director; or

- the total number of shares held by non-controlling, disinterested shareholders (as described in the preceding bullet point) that are voted against the election of the external director does not exceed 2% of the aggregate voting rights in the company.

The term controlling shareholder is defined in the Israeli Companies Law as a shareholder with the ability to direct the activities of the Company, other than by virtue of being an office holder. A person may not serve as an external director of a company if (i) such person is a relative of a controlling shareholder of a company or (ii) at the date of such person's appointment or within the prior two years, such person, such person's relative, partner, employer or any entity under such person's control or anyone to whom such person is subordinate, whether directly or indirectly, has or had any affiliation with (a) the company, (b) our controlling shareholder at the time of such person's appointment or (c) any entity that is either controlled by the company or under common control with the company at the time of such appointment or during the prior two years. If a company does not have a controlling shareholder or a shareholder who holds company shares entitling him to vote at least 25% of the votes in a shareholders meeting, then a person may not serve as an external director if, such person or such person's relative, partner, employer or any entity under such person's control, has or had, on or within the two years preceding the date of the person's appointment to serve as an external director, any affiliation with the chairman of our board of directors, chief executive officer, a substantial shareholder who holds at least 5% of the issued and outstanding shares of the company or voting rights which entitle him to vote at least 5% of the votes in a shareholders meeting, or the chief financial officer of the company.

The term affiliation includes:

- an employment relationship;

- a business or professional relationship even if not maintained on a regular basis (excluding insignificant relationships);

- control; and

- service as an office holder, excluding service as a director in a private company prior to the first offering of its shares to the public if such director was appointed as a director of the private company in order to serve as an external director following the public offering.

The term relative is defined as a spouse, sibling, parent, grandparent or descendant; a spouse's sibling, parent or descendant; and the spouse of each of the foregoing persons.

In addition, no person may serve as an external director if that person's professional activities create, or may create, a conflict of interest with that person's responsibilities as a director or otherwise interfere with that person's ability to serve as an external director or if the person is an employee of the Israel Securities Authority, or ISA, or of an Israeli stock exchange. Furthermore, a person may not continue to serve as an external director if he or she received direct or indirect compensation from the company for his or her role as a director. This prohibition does not apply to compensation paid or given in accordance with regulations promulgated under the Israeli Companies Law or amounts paid pursuant to indemnification and/or exculpation contracts or commitments and insurance coverage. If, at the time an external director is appointed, all current members of the board of directors not otherwise affiliated with the company are of the same gender, then that external director must be of the other gender. In addition, a director of a company may not be elected as an external director of another company if, at that time, a director of the other company is acting as an external director of the first company.

Following the termination of an external director's service on a board of directors, such former external director and his or her spouse and children may not be provided with a direct or indirect benefit by the company, its controlling shareholder or any entity under its controlling shareholder's control. This includes engagement to serve as an executive officer or director of the company or a company controlled by its controlling shareholder, or employment by, or providing services to, any such company for consideration, either directly or indirectly, including through a corporation controlled by the former external director, for a period of two years (and for a period of one year with respect to relatives of the former external director).

The Israeli Companies Law provides that an external director must meet certain professional qualifications or have financial and accounting expertise and that at least one external director must have financial and accounting expertise. However, if at least one of our other directors (i) meets the independence requirements of the Securities Exchange Act of 1934, as amended, (ii) meets the standards of the NYSE MKT rules for membership on the audit committee and (iii) has financial and accounting expertise as defined in the Israeli Companies Law and applicable regulations, then neither of our external directors is required to possess financial and accounting expertise as long as both possess other requisite professional qualifications. Our Board of Directors is required to determine whether a director possesses financial and accounting expertise by examining whether, due to the director's education, experience and qualifications, the director is highly proficient and knowledgeable with regard to business-accounting issues and financial statements, to the extent that the director is able to engage in a discussion concerning the presentation of financial information in our financial statements, among others. The regulations define a director with the requisite professional qualifications as a director who satisfies one of the following requirements: (i) the director holds an academic degree in either economics, business administration, accounting, law or public administration; (ii) the director either holds an academic degree in any other field or has completed another form of higher education in our primary field of business or in an area which is relevant to the office of an external director; or (iii) the director has at least five years of experience serving in any one of the following, or at least five years of cumulative experience serving in two or more of the following capacities: (a) a senior business management position in a corporation with a substantial scope of business; (b) a senior position in our primary field of business; or (c) a senior position in public administration.

The Israeli Companies Law defines an independent director as a director who complies with the following and was appointed as such in accordance with Chapter 1 of Part 56 of the Israeli Companies Law: (1) the director complies with the qualification to serve as an external director as set out in Sections 240 (b)-(f) of the Israeli Companies Law and the audit committee has approved such compliance; and (2) the director has not served as a director of the company for more than nine consecutive years (which, for such purpose, does not include breaks in such service for periods of less than two year).

If an external directorship becomes vacant and there are less than two external directors on the board of directors at the time, then the board of directors is required under the Israeli Companies Law to call a shareholders' meeting as soon as possible to appoint a replacement external director.

Each committee of the board of directors that is authorized to exercise the powers of the board of directors must include at least one external director, except that the audit committee and compensation committee must each include all external directors then serving on the board of directors. Under the Israeli Companies Law, external directors of a company are prohibited from receiving, directly or indirectly, any compensation for their services as external directors, other than compensation and reimbursement of expenses pursuant to applicable regulations promulgated under the Companies Law. Compensation of an external director is determined prior to his or her appointment and may not be changed during his or her term subject to certain exceptions.

Israel Shamay and Gil Oren serve as external directors on our Board of Directors pursuant to the provisions of the Israeli Companies Law. They both serve on our audit committee and our compensation committee. Our Board of Directors has determined that Gil Oren possesses accounting and financial expertise, and that both of our external directors possess the requisite professional qualifications. Guy Regev and Avi Sartani serve as independent directors on our Board of Directors. Guy Regev also serves on our audit committee and our compensation committee.

Audit Committee

The Israeli Companies Law requires public companies to appoint an audit committee. The responsibilities of the audit committee include identifying irregularities in the management of our business and approving related party transactions as required by law. An audit committee must consist of at least three directors, including all of its external directors and a majority of independent directors. The chairman of the board of directors, any director employed by or otherwise providing services to the company, and a controlling shareholder or any relative of a controlling shareholder, may not be a member of the audit committee. An audit committee may not approve an action or a transaction with a controlling shareholder, or with an office holder, unless at the time of approval two external directors are serving as members of the audit committee and at least one of the external directors was present at the meeting in which an approval was granted.

Our audit committee is currently comprised of three independent non-executive directors. The audit committee is chaired by Gil Oren, who serves as the audit committee financial expert, with Israel Shamay and Guy Regev as members. Our audit committee meets at least four times a year and monitors the adequacy of our internal controls, accounting policies and financial reporting. It regularly reviews the results of the ongoing risk self-assessment process, which we undertake, and our interim and annual reports prior to their submission for approval by the full Board of Directors. The audit committee oversees the activities of the internal auditor, sets its annual tasks and goals and reviews its reports. The audit committee reviews the objectivity and independence of the external auditors and also considers the scope of their work and fees.

Our audit committee provides assistance to our Board of Directors in fulfilling its legal and fiduciary obligations in matters involving our accounting, auditing, financial reporting, internal control and legal compliance functions by pre-approving the services performed by our independent accountants and reviewing their reports regarding our accounting practices and systems of internal control over financial reporting. Our audit committee also oversees the audit efforts of our independent accountants and takes those actions that it deems necessary to satisfy itself that the accountants are independent of management.

Under the Israeli Companies Law, our audit committee is responsible for (i) determining whether there are deficiencies in the business management practices of our company, including in consultation with our internal auditor or the independent auditor, and making recommendations to the Board of Directors to improve such practices and amend such deficiencies, (ii) determining whether certain related party transactions (including transactions in which an office holder has a personal interest) should be deemed as material or extraordinary, and to approve such transactions (which may be approved according to certain criteria set out by our audit committee on an annual basis) (see "— Approval of related party transactions under Israeli Law"), (iii) to establish procedures to be followed in respect of related party transactions with a controlling shareholder (where such are not extraordinary transactions), which may include, where applicable, the establishment of a competitive process for such transaction, under the supervision of the audit committee, or individual, or other committee or body selected by the audit committee, in accordance with criteria determined by the audit committee; (iv) to determine procedures for approving certain related party transactions with a controlling shareholder, which having been determined by the audit committee not to be extraordinary transactions, were also determined by the audit committee not to be negligible transactions; (v) where the Board of Directors approves the working plan of the internal auditor, to examine such working plan before its submission to the Board and propose amendments thereto, (iv) examining our internal controls and internal auditor's performance, including whether the internal auditor has sufficient resources and tools to dispose of its responsibilities, (v) examining the scope of our auditor's work and compensation and submitting a recommendation with respect thereto to our Board of Directors or shareholders, depending on which of them is considering the appointment of our auditor, and (vi) establishing procedures for the handling of employees' complaints as to the management of our business and the protection to be provided to such employees.

We have adopted a written charter for our audit committee, setting forth its responsibilities as outlined by the regulations of the SEC. In addition, our audit committee has adopted procedures for the receipt, retention and treatment of complaints we may receive regarding accounting, internal accounting controls or auditing matters and the submission by our employees of concerns regarding questionable accounting or auditing matters. In addition, SEC rules mandate that the audit committee of a listed issuer consist of at least three members, all of whom must be independent, as such term is defined by rules and regulations promulgated by the SEC. We are in compliance with the independence requirements of the SEC rules.

Any person who is not eligible to serve on the audit committee is further restricted from participating in its meetings and votes, unless the chairman of the audit committee determines that such person's presence is necessary in order to present a certain matter; provided, however, that company employees who are not controlling shareholders or relatives of such shareholders may be present in the meetings, but not for actual voting, and likewise, company counsel and secretary who are not controlling shareholders or relatives of such shareholders may be present in the meetings and for actual voting if such presence is requested by the audit committee.

In addition to the above, all such committee's members must apply with the following requirements:

- All members shall be members of the board of directors of the company.
- A t least one of the committee's members shall have financial and accounting expertise and the rest of the committee's members must have the ability to read and understand financial statements.

Our company, through our audit committee, is in full compliance with the above requirements.

Financial Statement Examination Committee

Under the Israeli Companies Law, the board of directors of a public company must appoint a financial statement examination committee, which consists of members with accounting and financial expertise or the ability to read and understand financial statements. According to a resolution of our Board of Directors, the audit committee has been assigned the responsibilities and duties of a financial statements examination committee, as permitted under relevant regulations promulgated under the Israeli Companies Law. From time to time as necessary and required to approve our financial statements, the audit committee holds separate meetings, prior to the scheduled meetings of the entire Board of Directors regarding financial statement approval. The function of a financial statements examination committee is to discuss and provide recommendations to its board of directors (including the report of any deficiency found) with respect to the following issues: (i) estimations and assessments made in connection with the preparation of financial statements; (ii) internal controls related to the financial statements; (iii) completeness and propriety of the disclosure in the financial statements; (iv) the accounting policies adopted and the accounting treatments implemented in material matters of the company; (v) value evaluations, including the assumptions and assessments on which evaluations are based and the supporting data in the financial statements. Our independent auditors and our internal auditors are invited to attend all meetings of audit committee when it is acting in the role of the financial statements examination committee.

Compensation Committee

Amendment no. 20 to the Companies Law was published on November 12, 2012 and became effective on December 12, 2012, or Amendment no. 20.In general, Amendment no. 20 requires public companies to appoint a compensation committee and to adopt a compensation policy with respect to its officers, or the Compensation Policy. In addition, Amendment no. 20 addresses the corporate approval process required for a public company's engagement with its officers (with specific reference to a director, a non-director officer, a chief executive officer and controlling shareholders and their relatives who are employed by the company).

The compensation committee shall be nominated by the board of directors and be comprised of its members. The compensation committee must consist of at least three members. All of the external directors must serve on the compensation committee and constitute a majority of its members. The remaining members of the compensation committee must be directors who qualify to serve as members of the audit committee (including the fact that they are independent) and their compensation should be identical to the compensation paid to the external directors of the company.

Similar to the rules that apply to the audit committee, the compensation committee may not include the chairman of the board, or any director employed by the company, by a controlling shareholder or by any entity controlled by a controlling shareholder, or any director providing services to the company, to a controlling shareholder or to any entity controlled by a controlling shareholder on a regular basis, or any director whose primary income is dependent on a controlling shareholder, and may not include a controlling shareholder or any of its relatives. Individuals who are not permitted to be compensation committee members may not participate in the committee's meetings other than to present a particular issue; provided, however, that an employee that is not a controlling shareholder or relative may participate in the committee's discussions, but not in any vote, and our legal counsel and corporate secretary may participate in the committee's discussions and votes if requested by the committee.

The roles of the compensation committee are, among others, to: (i) recommend to the board of directors the Compensation Policy for office holders and recommend to the board once every three years the extension of a Compensation Policy that had been approved for a period of more than three years; (ii) recommend to the directors any update of the Compensation Policy, from time to time, and examine its implementation; (iii) decide whether to approve the terms of office and of employment of office holders that require approval of the compensation committee; and (iv) decide, in certain circumstances, whether to exempt the approval of terms of office of a chief executive officer from the requirement of shareholder approval.

The compensation policy requires the approval of the general meeting of shareholders with a “Special Majority”, which requires a majority of the shareholders of the company who are not either a controlling shareholder or an "interested party" in the proposed resolution, or that shareholders holding less than 2% of the voting power in the company voted against the proposed resolution at such meeting. However, under special circumstances, the board of directors may approve the compensation policy without shareholder approval, if the compensation committee and thereafter the board of directors decided, based on substantiated reasons after they have reviewed the compensation policy again, that the compensation policy is in the best interest of the company.

Under the Israeli Companies Law, our compensation policy must generally serve as the basis for corporate approvals with respect to the financial terms of employment or engagement of office holders, including exemption, insurance, indemnification or any monetary payment or obligation of payment in respect of employment or engagement. The compensation policy must relate to certain factors, including advancement of the company's objective, the company's business plan and its long term strategy, and creation of appropriate incentives for office holders. It must also consider, among other things, the company's risk management, size and nature of its operations. The compensation policy must furthermore consider the following additional factors:

- The knowledge, skills, expertise, and accomplishments of the relevant office holder;
- The office holder's roles and responsibilities and prior compensation agreements with him or her;
- The relationship between the terms offered and the average compensation of the other employees of the company, including those employed through manpower companies;
- The impact of disparities in salary upon work relationships in the company;
- The possibility of reducing variable compensation at the discretion of the board of directors; the possibility of setting a limit on the exercise value of non-cash variable equity-based compensation; and
- As to severance compensation, the period of service of the office holder, the terms of his or her compensation during such service period, the company's performance during that period of service, the person's contributions towards the company's achievement of its goals and the maximization of its profits, and the circumstances under which the person is leaving the company.

The Compensation Policy must also include the following principles:

- the link between variable compensation and the long term performance and measurable criteria;
- the relationship between variable and fixed compensation, and the ceiling for the value of variable compensation;

- the conditions under which an office holder would be required to repay compensation paid to him or her if it was later shown that the data upon which such compensation was based was inaccurate and was required to be restated in the company's financial statements;

- the minimum holding or vesting period for variable, equity-based compensation; and

- maximum limits for severance compensation.

The Compensation Policy was approved by the general meeting of shareholders after discussions and recommendation of the compensation committee and approval by the Board of Directors on January 6, 2014. Moreover, the approval of the compensation committee is required in order to approve terms of office and/or employment of office holders.

Mr. Gil Oren is the chairman of our compensation committee. Mr. Israel Shamay and Mr. Guy Regev serve as the other members of our compensation committee.

Approval of Related Party Transactions under the Israeli Companies Law

Fiduciary duties of the office holders

The Israeli Companies Law imposes a duty of care and a duty of loyalty on all office holders of a company. The duty of care of an office holder is based on the duty of care set forth in connection with the tort of negligence under the Israeli Torts Ordinance (New Version) 5728-1968. This duty of care requires an office holder to act with the degree of proficiency with which a reasonable office holder in the same position would have acted under the same circumstances. The duty of care includes a duty to use reasonable means, in light of the circumstances, to obtain:

- information on the advisability of a given action brought for his or her approval or performed by virtue of his or her position; and

- all other important information pertaining to these action

The duty of loyalty requires an office holder to act in good faith and for the benefit of the company, and includes the duty to:

- refrain from any act involving a conflict of interest between the performance of his or her duties in the company and his or her other duties or personal affairs;

- refrain from any activity that is competitive with the business of the company;

- refrain from exploiting any business opportunity of the company for the purpose of gaining a personal advantage for himself or herself or others; and

- disclose to the company any information or documents relating to our affairs which the office holder received as a result of his or her position as an office holder.

We may approve an act performed in breach of the duty of loyalty of an office holder provided that the office holder acted in good faith, the act or its approval does not harm the company, and the office holder discloses his or her personal interest, as described below.

Disclosure of personal interests of an office holder and approval of acts and transactions

The Israeli Companies Law requires that an office holder promptly disclose to the company any personal interest that he or she may have and all related material information or documents relating to any existing or proposed transaction by the company. An interested office holder’s disclosure must be made promptly and in any event no later than the first meeting of the board of directors at which the transaction is considered. An office holder is not obligated to disclose such information if the personal interest of the office holder derives solely from the personal interest of his or her relative in a transaction that is not considered as an extraordinary transaction.

The term personal interest is defined under the Israeli Companies Law to include the personal interest of a person in an action or in the business of a company, including the personal interest of such person's relative or the interest of any corporation in which the person is an interested party, but excluding a personal interest stemming solely from the fact of holding shares in the company. A personal interest furthermore includes the personal interest of a person for whom the office holder holds a voting proxy or the interest of the office holder with respect to his or her vote on behalf of the shareholder for whom he or she holds a proxy even if such shareholder itself has no personal interest in the approval of the matter. An office holder is not, however, obliged to disclose a personal interest if it derives solely from the personal interest of his or her relative in a transaction that is not considered an extraordinary transaction.

Under the Israeli Companies Law, an extraordinary transaction which requires approval is defined as any of the following:

- a transaction other than in the ordinary course of business;
- a transaction that is not on market terms; or
- a transaction that may have a material impact on our profitability, assets or liabilities.

Under the Israeli Companies Law, once an office holder has complied with the disclosure requirement described above, a company may approve a transaction between the company and the office holder or a third party in which the office holder has a personal interest, or approve an action by the office holder that would otherwise be deemed a breach of duty of loyalty. However, a company may not approve a transaction or action that is adverse to our interest or that is not performed by the office holder in good faith.

Under the Companies Law, unless the articles of association of a company provide otherwise, a transaction with an office holder, a transaction with a third party in which the office holder has a personal interest, and an action of an office holder that would otherwise be deemed a breach of duty of loyalty requires approval by the board of directors. Our Articles of Association do not provide otherwise. If the transaction or action considered is (i) an extraordinary transaction, (ii) an action of an office holder that would otherwise be deemed a breach of duty of loyalty and may have a material impact on a company's profitability, assets or liabilities, (iii) an undertaking to indemnify or insure an office holder who is not a director, or (iv) for matters considered an undertaking concerning the terms of compensation of an office holder who is not a director, including, an undertaking to indemnify or insure such office holder, then approval by the audit committee is required prior to approval by the board of directors. Arrangements regarding the compensation, indemnification or insurance of a director require the approval of the audit committee, board of directors and shareholders, in that order.

A director who has a personal interest in a matter that is considered at a meeting of the board of directors or the audit committee may generally not be present at the meeting or vote on the matter, unless a majority of the directors or members of the audit committee have a personal interest in the matter or the chairman of the audit committee or board of directors, as applicable, determines that he or she should be present to present the transaction that is subject to approval. If a majority of the directors have a personal interest in the matter, such matter would also require approval of the shareholders of the company.

Disclosure of personal interests of a controlling shareholder and approval of transactions

Under the Israeli Companies Law and a recent amendment thereto, the disclosure requirements that apply to an office holder also apply to a controlling shareholder of a public company. See "— Audit Committee" for a definition of controlling shareholder. Extraordinary transactions with a controlling shareholder or in which a controlling shareholder has a personal interest, including a private placement in which a controlling shareholder has a personal interest, as well as transactions for the provision of services whether directly or indirectly by a controlling shareholder or his or her relative, or a company such controlling shareholder controls, and transactions concerning the terms of engagement of a controlling shareholder or a controlling shareholder's relative, whether as an office holder or an employee, require the approval of the audit committee, the board of directors and a majority of the shares voted by the shareholders of the company participating and voting on the matter in a shareholders' meeting. In addition, such shareholder approval must fulfill one of the following requirements:

- at least a majority of the shares held by shareholders who have no personal interest in the transaction and are voting at the meeting must be voted in favor of approving the transaction, excluding abstentions; or
- the shares voted by shareholders who have no personal interest in the transaction who vote against the transaction represent no more than 2% of the voting rights in the company.

To the extent that any such transaction with a controlling shareholder is for a period extending beyond three years, approval is required once every three years, unless the audit committee determines that the duration of the transaction is reasonable given the circumstances related thereto.

Duties of shareholders

Under the Israeli Companies Law, a shareholder has a duty to refrain from abusing its power in the company and to act in good faith and in an acceptable manner in exercising its rights and performing its obligations to the company and other shareholders, including, among other things, voting at general meetings of shareholders on the following matters:

- an amendment to the articles of association;
- an increase in our authorized share capital;
- a merger;
- an increase in our authorized share capital; and
- the approval of related party transactions and acts of office holders that require shareholder approval.

A shareholder also has a general duty to refrain from discriminating against other shareholders.

The remedies generally available upon a breach of contract will also apply to a breach of the above mentioned duties, and in the event of discrimination against other shareholders, additional remedies are available to the injured shareholder.

In addition, any controlling shareholder, any shareholder that knows that its vote can determine the outcome of a shareholder vote and any shareholder that, under a company's articles of association, has the power to appoint or prevent the appointment of an office holder, or has another power with respect to a company, is under a duty to act with fairness towards the company. The Israeli Companies Law does not describe the substance of this duty except to state that the remedies generally available upon a breach of contract will also apply in the event of a breach of the duty to act with fairness, taking the shareholder's position in the company into account.

Exculpation, Insurance and Indemnification of Directors and Officers

Under the Israeli Companies Law, a company may not exculpate an office holder from liability for a breach of the duty of loyalty. An Israeli company may exculpate an office holder in advance from liability to us, in whole or in part, for damages caused to us as a result of a breach of duty of care but only if a provision authorizing such exculpation is included in its articles of association. Our amended and restated articles of association include such a provision. We may not exculpate in advance a director from liability arising out of a prohibited dividend or distribution to shareholders.

Under the Israeli Companies Law and the Israeli Securities Law, a company may indemnify, or undertake in advance to indemnify, an office holder, provided its articles of association include a provision authorizing such indemnification, for the following liabilities and expenses imposed on an office holder or incurred by office holder due to acts performed by him or her as an office holder:

- Financial liability incurred by or imposed on him or her in favor of another person pursuant to a judgment, including a settlement or arbitrator's award approved by a court. However, if an undertaking to indemnify an office holder with respect to such liability is provided in advance, then such an undertaking must be limited to events which, in the opinion of the board of directors, can be foreseen based on our activities when the undertaking to indemnify is given, and to an amount or according to criteria determined by the board of directors as reasonable under the circumstances, and such undertaking shall detail the abovementioned foreseen events and amount or criteria;

- Reasonable litigation expenses, including attorneys' fees, incurred by the office holder as a result of an investigation or proceeding instituted against him or her by an authority authorized to conduct such investigation or proceeding, provided that (i) no indictment was filed against such office holder as a result of such investigation or proceeding; and (ii) no financial liability was imposed upon him or her as a substitute for the criminal proceeding as a result of such investigation or proceeding or, if such financial liability was imposed, it was imposed with respect to an offense that does not require proof of criminal intent or as a monetary sanction;

- Reasonable litigation expenses, including attorneys' fees, incurred by the office holder or imposed by a court in proceedings instituted against him or her by us, on our behalf, or by a third party, or in connection with criminal proceedings in which the office holder was acquitted, or as a result of a conviction for an offense that does not require proof of criminal intent; and

- Expenses, including reasonable litigation expenses and legal fees, incurred by an office holder in relation to an administrative proceeding instituted against such office holder, or certain compensation payments required to be made to an injured party, pursuant to certain provisions of the Israeli Securities Law.

Under the Israeli Companies Law, a company may insure an office holder against the following liabilities incurred for acts performed by him or her as an office holder if and to the extent provided in the Company's articles of association:

- a breach of the duty of loyalty to us, provided that the office holder acted in good faith and had a reasonable basis to believe that the act would not harm us;

- a breach of duty of care to us or to a third party; and

- a financial liability imposed on the office holder in favor of a third party.

Subject to the provisions of the Companies Law and the Securities Law, we may also enter into a contract to insure an office holder, in respect of expenses, including reasonable litigation expenses and legal fees, incurred by an office holder in relation to an administrative proceeding instituted against such office holder or payment required to be made to an injured party, pursuant to certain provisions of the Securities Law.

Nevertheless, under the Israeli Companies Law, a company may not indemnify, exculpate or insure an office holder against any of the following:

- a breach of fiduciary duty, except for indemnification and insurance for a breach of the duty of loyalty to us in the event office holder acted in good faith and had a reasonable basis to believe that the act would not prejudice us;
- a breach of duty of care committed intentionally or recklessly, excluding a breach arising out of the negligent conduct of the office holder;
- an act or omission committed with intent to derive unlawful personal benefit; or
- a fine, monetary sanction, penalty or forfeit levied against the office holder.

Under the Israeli Companies Law, exculpation, indemnification and insurance of office holders require the approval of the compensation committee, board of directors and, in certain circumstances, the shareholders. Our amended and restated articles of association permit us to exculpate, indemnify and insure our office holders to the fullest extent permitted by the Israeli Companies Law.

Approval of Compensation to Our Officers

The Israeli Companies Law prescribes that compensation to officers must be approved by a company's Board of Directors after obtaining the approval of the compensation committee.

As detailed above, our compensation committee consists of three independent directors: Israel Shamay, Gil Oren and Guy Regev. The responsibilities of the compensation committee are to set our overall policy on executive remuneration and to decide the specific remuneration, benefits and terms of employment for directors, officers and the Chief Executive Officer.

The objectives of the compensation committee's policies are that such individuals should receive compensation which is appropriate given their performance, level of responsibility and experience. Compensation packages should also allow us to attract and retain executives of the necessary caliber while, at the same time, motivating them to achieve the highest level of corporate performance in line with the best interests of shareholders. In order to determine the elements and level of remuneration appropriate to each executive director, the compensation committee reviews surveys on executive pay, obtains external professional advice and considers individual performance.

Internal Auditor

Under the Israeli Companies Law, the board of directors must appoint an internal auditor, nominated by the audit committee. The role of the internal auditor is to examine, among other matters, whether our actions comply with the law and orderly business procedure. Under the Israeli Companies Law, an internal auditor may not be:

- a person (or a relative of a person) who holds more than 5% of our shares;
- a person (or a relative of a person) who has the power to appoint a director or the general manager of the company;
- an executive officer or director of the company (or a relative thereof); or
- a member of our independent accounting firm, or anyone on his or her behalf.

We comply with the requirement of the Israeli Companies Law relating to internal auditors. Our internal auditors examine whether our various activities comply with the law and orderly business procedure. Our internal auditor is Daniel Spira C.P.A.

D. Employees.

As of December 31, 2014, we had eight employees, four of whom were employed in management and administration, three of whom were employed in research and development and two of whom were employed in management, research and development. All of these employees were located in Israel. As of December 21, 2013, we had nine employees.

While none of our employees are party to any collective bargaining agreements, certain provisions of the collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists' Associations) are applicable to our employees by order of the Israel Ministry of Labor. These provisions primarily concern the length of the workday, minimum daily wages for professional workers, pension fund benefits for all employees, insurance for work-related accidents, procedures for dismissing employees, determination of severance pay and other conditions of employment. We generally provide our employees with benefits and working conditions beyond the required minimums. We have never experienced any employment-related work stoppages and believe our relationship with our employees is good.

E. Share Ownership.

The following table sets forth information regarding the beneficial ownership of our outstanding ordinary shares as of March 23, 2015 by the members of our senior management, Board of Directors and 5% or more beneficial owners, individually and as a group. The beneficial ownership of ordinary shares is based on the 21,316,577 ordinary shares outstanding as of March 23, 2015 (which excludes 446,827 ordinary shares held in treasury) and is determined in accordance with the rules of the SEC and generally includes any ordinary shares over which a person exercises sole or shared voting or investment power. For purposes of the table below, we deem shares subject to options or warrants that are currently exercisable or exercisable within 60 days of March 23, 2015, to be outstanding and to be beneficially owned by the person holding the options or warrants for the purposes of computing the percentage ownership of that person but we do not treat them as outstanding for the purpose of computing the percentage ownership of any other person.

Name of Beneficial Owner	Number of Ordinary Shares	Percentage of Class*
Senior Management		
Ilan Cohn, PhD. *Chairman of the Board*	231,652(1)	1.1%
Pnina Fishman, PhD. *Chief Executive Officer and Director*	569,863(2)	2.6%
Motti Farbstein *Chief Operating Officer*	42,320(3)	*
Guy Regev *Director*	55,680(4)	*
Abraham Sartani, Ph.D. *Director*	12,346(5)	*
Gil Oren *Director*	2,500(6)	*
Directors and Executive Officers as a group (6 persons)	914,361	4.2%
5% or More Shareholders		
Empery Asset Management,LP	2,890,802(7)	12.9%
Cranshire Capital Advisors LLC	2,714,835(8)	12.2%

* Denotes less than 1%

(1) Includes (i) 133,567 ordinary shares, (ii) 420,000 registered warrants (Series 9) to purchase 16,800 ordinary shares at an exercise price of NIS 0.85 per warrant and expiring on May 1, 2015, and (iii) 2,032,136 unregistered options to purchase 81,285 ordinary shares at an exercise price of NIS 1.247 per option and expiring on March 20, 2017. All such warrants and options are fully vested.

(2) Includes (i) 263,433 ordinary shares, (ii) 90,000 registered warrants (Series 9) to purchase 3,600 ordinary shares at an exercise price of NIS 0.85 per warrant and expiring on May 1, 2015, and (iii) 7,570,761 unregistered options to purchase 302,830 ordinary shares, of which 4,890,761 options have an exercise price of NIS 0.50 per option and expire on August 23, 2016 and 2,680,000 options have an exercise price of NIS 0.644 per option and expire on January 13, 2021. All such warrants and options are fully vested.

(3) Includes (i) 1,133 ordinary shares, (ii) 1,014,062 unregistered options to purchase 40,562 ordinary shares, of which (1) 322,175 are exercisable into 12,887 ordinary shares at an exercise price of NIS 0.45 per option and expire on November 29, 2015, (2) 554,387 are exercisable into 22,175 ordinary shares at an exercise price of NIS 0.307 per option and expire on November 26, 2018, (3) 81,250 are exercisable into 3,250 ordinary shares at an exercise price of NIS 0.385 per option and expire on May 2, 2022, and (4) 56,250 are exercisable into 2,250 ordinary shares at an exercise price of NIS 0.326 per option and expire on March 20, 2023, and (iii) 625 unregistered options to purchase 625 ordinary shares at an exercise price of NIS 8.118 per option and expire on March 18, 2025. All such options are fully vested or will vest within 60 days from March 23, 2015.Excludes 62,500 unregistered options to purchase 2,500ordinary shares and 9,375 unregistered options to purchase 9,375 ordinary shares that vest in more than 60 days from March 23, 2015..

(4) Includes (i) 24,240 ordinary shares, (ii) 36,000 registered warrants (Series 9) to purchase 1,440 ordinary shares at an exercise price of NIS 0.85 per warrant and expiring on May 1, 2015, (iii) 250,000 registered warrants (Series 10) to purchase 10,000 ordinary shares at an exercise price of NIS 0.394 per warrant and expiring on October 31, 2015, (iv) 250,000 registered warrants (Series 11) to purchase 10,000 ordinary shares at an exercise price of NIS 0.392 per warrant and expiring on April 30, 2016, and (v) 250,000 unregistered options are exercisable into 10,000 ordinary shares at an exercise price of NIS 0.60 per option and expire on May 2, 2023. All such warrants and options are fully vested or will vest within 60 days from March 23, 2015.

(5) Includes (i) 613 ordinary shares, and (ii) 293,305 unregistered options to purchase 11,733 ordinary shares, of which 193,305 are exercisable into 7,732 ordinary shares at an exercise price of NIS 0.45 per option and expire on August 23, 2016, and 100,000 are exercisable into 4,000 ordinary shares at an exercise price of NIS 0.385 per option and expire on August 14, 2022. All such options are fully vested.

(6) Includes 2,500 unregistered options to purchase 2,500 ordinary shares at an exercise price of NIS 12 per option and expire on July 14, 2024.Excludes 7,500 unregistered options to purchase 7,500 ordinary shares that vest in more than 60 days from March 23, 2015.

(7) Represents (i) 73,298 American Depositary Shares, or ADSs, representing 146,596 ordinary shares held by Empery Tax Efficient, LP ("ETE I Fund"), (ii) 540,332 ADSs representing 1,080,664 ordinary shares held by Empery Tax Efficient II, LP ("ETE II Fund"), (iii) 285,246 ADSs representing 570,492 ordinary shares held by Empery Asset Master Ltd ("EAM Fund" and together with the ETE I Fund and ETE II Fund, the "Empery Funds"), (iv) warrants to purchase 85,193 ADSs representing 170,385 ordinary shares held by ETE I Fund, (v) warrants to purchase 270,166 ADSs representing 540,332 ordinary shares held by ETE II Fund, and (vi) warrants to purchase 191,167 ADSs representing 382,333 ordinary shares held by EAM Fund. Empery Asset Management, LP (the "Investment Manager"), serves as investment manager of the Empery Funds. Each of Ryan M. Lane and Martin D. Hoe is a Managing Member of Empery AM GP, LLC, the general partner of the Investment Manager. Pursuant to the terms of the foregoing warrants the holders cannot exercise such warrants if they would beneficially own, after any such exercise, more than 4.99% of the outstanding ordinary shares. The percentage in the table above does not give effect to the blocker. The foregoing information is based in part on a Schedule 13G filed with the SEC on December 5, 2014 by ETE II Fund, the Investment Manager, Mr. Lane and Mr. Hoe.

(8) Represents (i) 898,877 ADSs representing 1,797,754 ordinary shares held by Equitec Specialists, LLC ("Equitec"), (ii) warrants to purchase 458,541 ADSs representing 917,081 ordinary shares held by Equitec, and (iii) warrants to purchase 27,306 ADSs representing 54,612 ordinary shares held by Cranshire Capital Master Fund, Ltd. ("Cranshire Master Fund").Cranshire Capital Advisors, LLC ("CCA") is the investment manager of Cranshire Capital Master Fund. and has voting control and investment discretion over securities held by Cranshire Master Fund. Mitchell P. Kopin, the sole member and the sole member of the Board of Managers of CCA, has voting control over CCA. As a result, each of Mr. Kopin and CCA may be deemed to have beneficial ownership (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended) of the securities held by Cranshire Master Fund. CCA is the investment manager of Equitec and has voting control and investment discretion over securities held in the managed accounts by Equitec. Mr. Kopin, the sole member and the sole member of the Board of Managers of CCA, has voting control over CCA. As a result, each of Mr. Kopin and CCA may be deemed to have beneficial ownership (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended) of the securities held in the managed accounts by Equitec.Pursuant to the terms of the foregoing warrants the holders cannot exercise such warrants if they would beneficially own, after any such exercise, more than 4.99% of the outstanding ordinary shares. The percentage in the table above does not give effect to the blocker. The foregoing information is based on our information and belief.

Share Option Plans

We maintain the following share option plans for our and our subsidiary's employees, directors and consultants. In addition to the discussion below, see Note 14b of our consolidated financial statements, included in "Item 18. Financial Statements."

Our Board of Directors administers our share option plans and has the authority to designate all terms of the options granted under our plans including the grantees, exercise prices, grant dates, vesting schedules and expiration dates, which may be no more than ten years after the grant date. Options may not be granted with an exercise price of less than the fair market value of our ordinary shares on the date of grant, unless otherwise determined by our Board of Directors.

As of December 31, 2014, we have granted to employees, directors and consultants options that are outstanding to purchase up to 1,094,732 ordinary shares, par value NIS 0.25, pursuant to the 2003 and 2013 share option plans, or the 2003 and 2013 Plans, and pursuant to certain grants apart from these plans also discussed below under Non-Plan Share Options.

2003 Share Option Plan

Under the 2003 Plan we granted options during the period between 2003 and 2013, at exercise prices between NIS 0.25 and NIS 31.175 per ordinary share, par value NIS 0.25. Options to purchase up to 1,132,514 ordinary shares, par value NIS 0.25, were available to be granted under the 2003 Plan. As of December 31, 2014, 14,567,790 options to purchase 582,707 ordinary shares were outstanding. Options granted to Israeli employees were in accordance with section 102 of the Income Tax Ordinance, 1961, or the Tax Ordinance, under the capital gains option set forth in section 102(b)(2) of the Tax Ordinance. The options are non-transferable.

The option term is for a period of ten years from the grant date. The options were granted for no consideration. The options vest over a four or two year period. As of December 31, 2014, options to purchase 564,857 ordinary shares, par value NIS 0.25, were fully vested.

2013 Share Option Plan

Under the 2013 Plan we granted options from 2014, at exercise price of NIS 12 per ordinary share, par value NIS 0.25. Options to purchase up to 1,000,000 ordinary shares, par value NIS 0.25, were available to be granted under the 2013 Plan. As of December 31, 2014, 10,000 options to purchase 10,000 ordinary shares were outstanding. Options granted to Israeli employees were in accordance with section 102 of the Income Tax Ordinance, 1961, or the Tax Ordinance, under the capital gains option set forth in section 102(b)(2) of the Tax Ordinance. The options are non-transferable.

The option term is for a period of ten years from the grant date. The options were granted for no consideration. The options vest over a three year period. As of December 31, 2014, options to purchase 833 ordinary shares, par value NIS 0.25, were fully vested.

Non-Plan Share Options

In addition to the options granted under our share option plans, at December 31, 2014, there were outstanding and exercisable options to purchase 502,026 ordinary shares, par value NIS 0.25, which had been granted to an investor, not under the 2003 Plan. The options were granted at exercise price of NIS 15 per ordinary share, par value NIS 0.25. As of December 31, 2014, these options were fully vested. The options were extended by one year till October 21, 2015.

ITEM 7. Major Shareholders and Related Party Transactions

A. Major Shareholders.

The beneficial ownership of 5% or more holders is set forth in the beneficial ownership table set forth above under "Item 6 E. Share Ownership."

On June 17, 2013, OphthaliX sold 268,095 ordinary shares on the TASE, for aggregate consideration of US$510,714. After such sale, OphthaliX owns 446,827 ordinary shares of our company.

To our knowledge, as of March 23,2015 there were approximately three shareholders of record with a United States address which held 102,000 ordinary shares, directly or represented by ADSs, representing in the aggregate approximately 0.5%of our then outstanding share capital. These numbers are not representative of the number of beneficial holders of our ordinary shares.

B. Related Party Transactions.

The following is a description of the transactions with related parties to which we, or our subsidiaries, are party, and which were in effect within the past three fiscal years. The descriptions provided below are summaries of the terms of such agreements, do not purport to be complete and are qualified in their entirety by the complete agreements.

We believe that we have executed all of our transactions with related parties on terms no less favorable to us than those we could have obtained from unaffiliated third parties. We are required by Israeli law to ensure that all future transactions between us and our officers, directors and principal shareholders and their affiliates are approved by a majority of our Board of Directors, including a majority of the independent and disinterested members of our Board of Directors, and that they are on terms no less favorable to us than those that we could obtain from unaffiliated third parties.

Employment and Consulting Agreements

We have or have had employment, consulting or related agreements with each member of our senior management. See "Item 6. Directors, Senior Management and Employees—Compensation—Employment and Consulting Agreements".

Indemnification Agreements

Our Articles of Association permit us to exculpate, indemnify and insure our directors and officeholders to the fullest extent permitted by the Israeli Companies Law. We have obtained directors' and officers' insurance for each of our officers and directors and have entered into indemnification agreements with all of our current officers and directors.

Agreements with Subsidiaries

See "Item 10. Additional Information—Material Contracts—OphthaliX Agreements" for a description of agreements with OphthaliX and Eye-Fite.

C. Interests of Experts and Counsel.

Not applicable.

ITEM 8. Financial Information

A. Consolidated Financial Statements and Other Financial Information

See "Item 18. Financial Statements" for a list of all financial statements filed as part of this Annual Report on Form 20-F.

Legal Matters

We are not involved in any legal or arbitration proceedings that may have or have had in the recent past, significant effects on our financial position or profitability.

Dividend Policy

We have never declared or paid cash dividends to our shareholders. Currently we do not intend to pay cash dividends. We intend to reinvest any earnings in developing and expanding our business. Any future determination relating to our dividend policy will be at the discretion of our Board of Directors and will depend on a number of factors, including future earnings, our financial condition, operating results, contractual restrictions, capital requirements, business prospects, applicable Israeli law and other factors our Board of Directors may deem relevant.

B. Significant Changes

See "Note 22:- Subsequent Events" to our consolidated financial statements included in this Annual Report beginning on page F-1 for a discussion of significant events that have occurred since December 31, 2014.

ITEM 9. The Offer and Listing

A. Offer and Listing Details

Ordinary Shares

Our ordinary shares have been trading on the Tel Aviv Stock Exchange, or TASE, under the symbol "CFBI" since October 2005.

The following table sets forth, for the periods indicated, the reported high and low closing sale prices of our ordinary shares on the TASE in NIS and U.S. dollars. U.S. dollar per ordinary share amounts were calculated using the U.S. dollar representative rate of exchange on the date to which the high or low market price is applicable, as reported by the Bank of Israel. As of December 31, 2014, we had 21,316,577 ordinary shares outstanding as of (which excludes 446,827 ordinary shares held in treasury) ordinary shares outstanding. See "Item 10—Additional Information—Memorandum and Articles of Association" for a detailed description of the rights attaching to the shares.

We effected a 1-for-25 reverse share split with respect to our ordinary shares, options and warrants on May 12, 2013. Reported prices in the table below have been adjusted to give retroactive effect to the share split.

	NIS		U.S.$	
	Price Per Ordinary Share (1)		Price Per Ordinary Share (1)	
	High	Low	High	Low
Annual:				
2014	11.140	4.495	3.198	1.175
2013	15.600	6.217	4.453	1.725
2012	12.400	7.325	3.225	1.800
2011	23.000	9.125	6.350	2.450
2010	19.000	11.800	5.225	3.100
Quarterly:				
Fourth Quarter 2014	9.350	4.495	2.341	1.175
Third Quarter 2014	7.068	6.023	1.985	1.634
Second Quarter 2014	10.480	6.018	3.018	1.749
First Quarter 2014	11.140	8.683	3.198	2.482
Fourth Quarter 2013	15.600	9.700	4.453	2.789
Third Quarter 2013	8.571	6.217	2.423	1.725
Second Quarter 2013	8.450	6.752	2.336	1.859
First Quarter 2013	10.825	8.000	2.900	2.198
Most Recent Six Months:				
March 2015 (through March 23, 2015)	10.099	8.267	2.735	2.059
February 2015	8.499	6.493	2.161	1.650
January 2015	7.728	6.310	1.953	1.582
December 2014	9.350	6.770	2.341	1.721
November 2014	8.800	4.495	2.296	1.175
October 2014	6.042	5.350	1.645	1.425
September 2014	7.068	6.023	1.958	1.634

(1) We effected a 1-for-25 reverse share split with respect to our ordinary shares, options and warrants on May 12, 2013. Reported prices in the table below have been adjusted to give retroactive effect to the share split.

On March 23, 2015, the last reported sales price of our ordinary shares on the TASE was NIS 10.099 per share, or $2.735 per share. On March 23, 2015, the exchange rate of the NIS to the dollar was $1.00 = NIS 4.018 as reported by the Bank of Israel.

For information with respect to our warrants, see “Item 5. Operating and Financial Review and Prospects—Warrants”.

ADSs

On October 2, 2012, our ADSs began trading over the counter, or OTC, in the United States under the symbol “CANFY” and on November 19, 2013, our ADSs began trading on the NYSE MKT under the symbol “CANF.” As of December 31, 2014, we had 4,629,617 ADSs outstanding. One ADS represents two ordinary shares. See “Item 12—Description of Securities Other Than Equity Securities—American Depositary Shares” for a description of the rights attaching to the ADSs.

The following table sets forth, for the periods indicated, the reported high and low closing sale prices of our ADSs on the OTC and Nasdaq Capital Market in U.S. dollars.

	U.S.$ Price Per ADS (1)	
	High	**Low**
Annual:		
2014	6.50	2.41
2013	8.60	3.30
2012 (from October 2, 2012)	5.50	4.74
Quarterly:		
Fourth Quarter 2014	4.80	2.41
Third Quarter 2014	4.21	3.21
Second Quarter 2014	6.10	3.49
First Quarter 2014	6.50	4.85
Fourth Quarter 2013	8.60	5.54
Third Quarter 2013	5.03	3.30
Second Quarter 2013	5.15	3.87
First Quarter 2013	5.10	4.50
Most Recent Six Months:		
March 2015 (through March 23, 2015)	5.35	4.25
February 2015	4.67	3.18
January 2015	3.85	3.00
December 2014	4.62	3.35
November 2014	4.80	2.41
October 2014	3.28	2.78
September 2014	4.00	3.21

(1) We effected a 1-for-25 reverse share split with respect to our ordinary shares, options and warrants on May 12, 2013. Reported prices in the table below have been adjusted to give retroactive effect to the share split.

On March 23, 2015, the last reported sales price of our ADSs on the NYSE MKT was $5.35 per share.

B. Plan of Distribution.

Not applicable.

C. Markets.

See "—Offer and Listing Details" above.

D. Selling Shareholders.

Not applicable.

E. Dilution.

Not applicable.

F. Expenses of the Issue.

Not applicable.

ITEM 10. Additional Information

A. Share Capital.

Not applicable.

B. Memorandum and Articles of Association.

Our number with the Israeli Registrar of Companies is 512022153. Our purpose is set forth in Section 3 of our Articles of Association and includes every lawful purpose.

Our ordinary shares that are fully paid for are issued in registered form and may be freely transferred under our Articles of Association, unless the transfer is restricted or prohibited by applicable law or the rules of a stock exchange on which the shares are traded. The ownership or voting of our ordinary shares by non-residents of Israel is not restricted in any way by our Articles of Association or the laws of the State of Israel, except for ownership by nationals of some countries that are, or have been, in a state of war with Israel.

Pursuant to the Israeli Companies Law and our Articles of Association, our Board of Directors may exercise all powers and take all actions that are not required under law or under our Articles of Association to be exercised or taken by our shareholders, including the power to borrow money for company purposes.

Our Articles of Association enable us to increase or reduce our share capital. Any such changes are subject to the provisions of the Israeli Companies Law and must be approved by a resolution duly passed by our shareholders at a general or special meeting by voting on such change in the capital. In addition, transactions that have the effect of reducing capital, such as the declaration and payment of dividends in the absence of sufficient retained earnings and profits and an issuance of shares for less than their nominal value, require a resolution of our Board of Directors and court approval.

Dividends

We may declare a dividend to be paid to the holders of our ordinary shares in proportion to their respective shareholdings. Under the Israeli Companies Law, dividend distributions are determined by the board of directors and do not require the approval of the shareholders of a company unless such company's articles of association provide otherwise. Our Articles of Association do not require shareholder approval of a dividend distribution and provide that dividend distributions may be determined by our Board of Directors.

Pursuant to the Israeli Companies Law, we may only distribute dividends from our profits accrued over the previous two years, as defined in the Israeli Companies Law, according to our then last reviewed or audited financial reports, or we may distribute dividends with court approval. In each case, we are only permitted to pay a dividend if there is no reasonable concern that payment of the dividend will prevent us from satisfying our existing and foreseeable obligations as they become due.

Election of Directors

Our ordinary shares do not have cumulative voting rights in the election of directors. As a result, the holders of a majority of the voting power represented at a shareholders meeting have the power to elect all of our directors, subject to the special approval requirements for external directors described under "Item 6. Directors, Senior Management and Employees — Board Practices — External Directors."

Pursuant to our Articles of Association, other than the external directors, for whom special election requirements apply under the Israeli Companies Law, our directors are elected at a general or special meeting of our shareholders and serve on the Board of Directors until the end of the next general meeting or they are removed by the majority of our shareholders at a general or special meeting of our shareholders or upon the occurrence of certain events, in accordance with the Israeli Companies Law and our Articles of Association. In addition, our Articles of Association allow our Board of Directors to appoint directors to fill vacancies on the Board of Directors to serve until the next general meeting or special meeting, or earlier if required by our Articles of Association or applicable law. We have held elections for each of our non-external directors at each annual meeting of our shareholders since our initial public offering in Israel. External directors are elected for an initial term of three years and may be removed from office pursuant to the terms of the Israeli Companies Law. See "Item 6. Directors, Senior Management and Employees — Board Practices — External Directors."

Shareholder Meetings

Under Israeli law, we are required to hold an annual general meeting of our shareholders once every calendar year that must be no later than 15 months after the date of the previous annual general meeting. All meetings other than the annual general meeting of shareholders are referred to as special meetings. Our Board of Directors may call special meetings whenever it sees fit, at such time and place, within or outside of Israel, as it may determine. In addition, the Israeli Companies Law and our Articles of Association provide that our Board of Directors is required to convene a special meeting upon the written request of (i) any two of our directors or one quarter of our Board of Directors or (ii) one or more shareholders holding, in the aggregate, either (1) 5% of our outstanding shares and 1% of our outstanding voting power or (2) 5% of our outstanding voting power.

Subject to the provisions of the Israeli Companies Law and the regulations promulgated thereunder, shareholders entitled to participate and vote at general meetings are the shareholders of record on a date to be decided by the board of directors, which may be between four and forty days prior to the date of the meeting. Furthermore, the Israeli Companies Law and our Articles of Association require that resolutions regarding the following matters must be passed at a general meeting of our shareholders:

- amendments to our Articles of Association;
- appointment or termination of our auditors;
- appointment of directors and appointment and dismissal of external directors;
- approval of acts and transactions requiring general meeting approval pursuant to the Israeli Companies Law;
- director compensation, indemnification and change of the principal executive officer;
- increases or reductions of our authorized share capital;
- a merger; and
- the exercise of our Board of Director's powers by a general meeting, if our Board of Directors is unable to exercise its powers and the exercise of any of its powers is required for our proper management.

The Israeli Companies Law requires that a notice of any annual or special shareholders meeting be provided at least 21 days prior to the meeting and if the agenda of the meeting includes the appointment or removal of directors, the approval of transactions with office holders or interested or related parties, or an approval of a merger, notice must be provided at least 35 days prior to the meeting.

The Israeli Companies Law does not allow shareholders of publicly traded companies to approve corporate matters by written consent. Consequently, our Articles of Association does not allow shareholders to approve corporate matters by written consent.

Pursuant to our Articles of Association, holders of our ordinary shares have one vote for each ordinary share held on all matters submitted to a vote before the shareholders at a general meeting.

Quorum

The quorum required for our general meetings of shareholders consists of at least two shareholders present in person, by proxy or written ballot who hold or represent between them at least 25% of the total outstanding voting rights.

A meeting adjourned for lack of a quorum is adjourned to the same day in the following week at the same time and place or on a later date if so specified in the summons or notice of the meeting. At the reconvened meeting, any number of our shareholders present in person or by proxy shall constitute a lawful quorum.

Resolutions

Our Articles of Association provide that all resolutions of our shareholders require a simple majority vote, unless otherwise required by applicable law.

Israeli law provides that a shareholder of a public company may vote in a meeting and in a class meeting by means of a written ballot in which the shareholder indicates how he or she votes on resolutions relating to the following matters:

- an appointment or removal of directors;
- an approval of transactions with office holders or interested or related parties;
- an approval of a merger or any other matter in respect of which there is a provision in the articles of association providing that decisions of the general meeting may also be passed by written ballot;
- authorizing the chairman of the board of directors or his relative to act as our chief executive officer or act with such authority; or authorize our chief executive officer or his relative to act as the chairman of the board of directors or act with such authority; and
- other matters which may be prescribed by Israel's Minister of Justice.

The provision allowing the vote by written ballot does not apply where the voting power of the controlling shareholder is sufficient to determine the vote. Our Articles of Association provides that our Board of Directors may prevent voting by means of a written ballot and this determination is required to be stated in the notice convening the general meeting.

The Israeli Companies Law provides that a shareholder, in exercising his or her rights and performing his or her obligations toward the company and its other shareholders, must act in good faith and in a customary manner, and avoid abusing his or her power. This is required when voting at general meetings on matters such as changes to the articles of association, increasing our registered capital, mergers and approval of related party transactions. A shareholder also has a general duty to refrain from depriving any other shareholder of its rights as a shareholder. In addition, any controlling shareholder, any shareholder who knows that its vote can determine the outcome of a shareholder vote and any shareholder who, under such company's articles of association, can appoint or prevent the appointment of an office holder, is required to act with fairness towards the company. The Israeli Companies Law does not describe the substance of this duty except to state that the remedies generally available upon a breach of contract will also apply to a breach of the duty to act with fairness, and, to the best of our knowledge, there is no binding case law that addresses this subject directly.

Under the Israeli Companies Law, unless provided otherwise in a company's articles of association, a resolution at a shareholders meeting requires approval by a simple majority of the voting rights represented at the meeting, in person, by proxy or written ballot, and voting on the resolution. A resolution for the voluntary winding up of the company requires the approval of holders of 75% of the voting rights represented at the meeting, in person, by proxy or by written ballot and voting on the resolution.

In the event of our liquidation, after satisfaction of liabilities to creditors, our assets will be distributed to the holders of our ordinary shares in proportion to their shareholdings. This right, as well as the right to receive dividends, may be affected by the grant of preferential dividend or distribution rights to the holders of a class of shares with preferential rights that may be authorized in the future.

Access to Corporate Records

Under the Israeli Companies Law, all shareholders of a company generally have the right to review minutes of our general meetings, its shareholders register and principal shareholders register, articles of association, financial statements and any document it is required by law to file publicly with the Israeli Companies Registrar and the ISA. Any of our shareholders may request access to review any document in our possession that relates to any action or transaction with a related party, interested party or office holder that requires shareholder approval under the Israeli Companies Law. We may deny a request to review a document if we determine that the request was not made in good faith, that the document contains a commercial secret or a patent or that the document's disclosure may otherwise prejudice our interests.

Acquisitions under Israeli Law

Full Tender Offer

A person wishing to acquire shares of a public Israeli company and who would as a result hold over 90% of the target company's issued and outstanding share capital is required by the Israeli Companies Law to make a tender offer to all of our shareholders for the purchase of all of the issued and outstanding shares of the company. A person wishing to acquire shares of a public Israeli company and who would as a result hold over 90% of the issued and outstanding share capital of a certain class of shares is required to make a tender offer to all of the shareholders who hold shares of the same class for the purchase of all of the issued and outstanding shares of the same class. If the shareholders who do not accept the offer hold less than 5% of the issued and outstanding share capital of the company or of the applicable class, all of the shares that the acquirer offered to purchase will be transferred to the acquirer by operation of law (provided that a majority of the offerees that do not have a personal interest in such tender offer shall have approved the tender offer except that if the total votes to reject the tender offer represent less than 2% of the company's issued and outstanding share capital, in the aggregate, approval by a majority of the offerees that do not have a personal interest in such tender offer is not required to complete the tender offer). However, a shareholder that had its shares so transferred may petition the court within six months from the date of acceptance of the full tender offer, whether or not such shareholder agreed to the tender or not, to determine whether the tender offer was for less than fair value and whether the fair value should be paid as determined by the court unless the acquirer stipulated in the tender offer that a shareholder that accepts the offer may not seek appraisal rights. If the shareholders who did not accept the tender offer hold 5% or more of the issued and outstanding share capital of the company or of the applicable class, the acquirer may not acquire shares of the company that will increase its holdings to more than 90% of our issued and outstanding share capital or of the applicable class from shareholders who accepted the tender offer.

Special Tender Offer

The Israeli Companies Law provides that an acquisition of shares of a public Israeli company must be made by means of a special tender offer if as a result of the acquisition the purchaser would become a holder of 25% or more of the voting rights in the company, unless one of the exemptions in the Israeli Companies Law is met. This rule does not apply if there is already another holder of at least 25% of the voting rights in the company. Similarly, the Israeli Companies Law provides that an acquisition of shares in a public company must be made by means of a tender offer if as a result of the acquisition the purchaser would become a holder of 45% or more of the voting rights in the company, if there is no other shareholder of the company who holds 45% or more of the voting rights in the company, unless one of the exemptions in the Israeli Companies Law is met.

A special tender offer must be extended to all shareholders of a company but the offeror is not required to purchase shares representing more than 5% of the voting power attached to our outstanding shares, regardless of how many shares are tendered by shareholders. A special tender offer may be consummated only if (i) at least 5% of the voting power attached to our outstanding shares will be acquired by the offeror and (ii) the number of shares tendered in the offer exceeds the number of shares whose holders objected to the offer.

If a special tender offer is accepted, then the purchaser or any person or entity controlling it or under common control with the purchaser or such controlling person or entity may not make a subsequent tender offer for the purchase of shares of the target company and may not enter into a merger with the target company for a period of one year from the date of the offer, unless the purchaser or such person or entity undertook to effect such an offer or merger in the initial special tender offer.

Merger

The Israeli Companies Law permits merger transactions if approved by each party's board of directors and, unless certain requirements described under the Israeli Companies Law are met, a majority of each party's shares voted on the proposed merger at a shareholders' meeting called with at least 35 days' prior notice.

For purposes of the shareholder vote, unless a court rules otherwise, the merger will not be deemed approved if a majority of the shares represented at the shareholders meeting that are held by parties other than the other party to the merger, or by any person who holds 25% or more of the outstanding shares or the right to appoint 25% or more of the directors of the other party, vote against the merger. If the transaction would have been approved but for the separate approval of each class or the exclusion of the votes of certain shareholders as provided above, a court may still approve the merger upon the request of holders of at least 25% of the voting rights of a company, if the court holds that the merger is fair and reasonable, taking into account the value of the parties to the merger and the consideration offered to the shareholders.

Upon the request of a creditor of either party to the proposed merger, the court may delay or prevent the merger if it concludes that there exists a reasonable concern that, as a result of the merger, the surviving company will be unable to satisfy the obligations of any of the parties to the merger, and may further give instructions to secure the rights of creditors.

In addition, a merger may not be completed unless at least 50 days have passed from the date that a proposal for approval of the merger was filed by each party with the Israeli Registrar of Companies and 30 days have passed from the date the merger was approved by the shareholders of each party.

Antitakeover Measures

The Israeli Companies Law allows us to create and issue shares having rights different from those attached to our ordinary shares, including shares providing certain preferred rights, distributions or other matters and shares having preemptive rights. As of the date of this annual report, we do not have any authorized or issued shares other than our ordinary shares. In the future, if we do create and issue a class of shares other than ordinary shares, such class of shares, depending on the specific rights that may be attached to them, may delay or prevent a takeover or otherwise prevent our shareholders from realizing a potential premium over the market value of their ordinary shares. The authorization of a new class of shares will require an amendment to our Articles of Association which requires the prior approval of the holders of a majority of our shares at a general meeting. In addition, the rules and regulations of the TASE also limit the terms permitted with respect to a new class of shares and prohibit any such new class of shares from having voting rights. Shareholders voting in such meeting will be subject to the restrictions provided in the Israeli Companies Law as described above.

Borrowing Powers

Under the Israeli Companies Law and our amended and restated articles of association, our Board of Directors may exercise all powers and take all actions that are not required under law or under our amended and restated articles of association to be exercised or taken by our shareholders or other corporate bodies, including the power to borrow money for company purposes.

Changes in Capital

Our amended and restated articles of association enable us to increase or reduce our share capital. Any such changes are subject to the provisions of the Israeli Companies Law and must be approved by a resolution duly passed by our shareholders at a general meeting by voting on such change in the capital. In addition, transactions that have the effect of reducing capital, such as the declaration and payment of dividends in the absence of sufficient retained earnings or profits and, in certain circumstances, an issuance of shares for less than their nominal value, require the approval of both our Board of Directors and an Israeli court.

C. Material Contracts.

The following are summary descriptions of certain material agreements to which we are a party. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this Annual Report on Form 20-F.

OphthaliX Agreements

On November 21, 2011, we consummated a series of transactions resulting in the acquisition of 82.3% of the issued and outstanding share capital of OphthaliX, Inc., a Delaware corporation (formerly, Denali Concrete Management Inc., a Nevada corporation), whose common shares are traded in the United States on the OTC under the symbol "OPLI".

The transactions were consummated pursuant to a series of agreements that we executed on November 21, 2011 with OphthaliX to spin-off our activity in the ophthalmology field to OphthaliX, or the Spin-Off Agreements. Prior to entering into the Spin-Off Agreements, we obtained a pre-ruling from the Israeli Tax Authority which prohibits us from selling more than 10% of the OphthaliX common stock that we hold until at least November 21, 2013. If we sell any of such shares prior to such date, we will be subject to a significant tax by the Israeli Tax Authority. As of December 31, 2014, we did not sell any of such shares.

Spin-Off Agreements

Pursuant to the Spin-Off Agreements, we formed Eye-Fite as a wholly-owned subsidiary of ours and transferred to all of the issued and outstanding share capital of Eye-Fite to OphthaliX, such that Eye-Fite became a wholly-owned subsidiary of OphthaliX. In consideration for the transfer of Eye-Fite, OphthaliX issued us 8,000,000 shares of OphthaliX common stock, which represented 86.7% of the issued and outstanding share capital of OphthaliX. In addition to the 8,000,000 shares of OphthaliX common stock that were issued to us in consideration for the transfer of Eye-Fite, we also acquired (i) 466,139 shares of OphthaliX common stock that were issued to us in exchange for 714,922 of our ordinary shares, which reflected a price of $5.148 per share of OphthaliX common stock, and (ii) 97,113 shares of OphthaliX common stock that were issued to us as consideration for our investment of $500,000 in OphthaliX, also at a price of $5.148 per share of OphthaliX common stock. We were also granted 1,267,316 warrants exercisable for 281,626 shares of OphthaliX common stock. Such warrants have an exercise price of US$7.74 per share and expire on November 20, 2016. As of March 23, 2015, none of the warrants had been exercised.

As a result of the Spin-Off Agreements, we appointed all of the members of the OphthaliX board of directors. According to the terms of the Spin-Off Agreements, OphthaliX will continue the development processes, clinical trials and registration of the ophthalmic indications of CF101.

As part of the acquisition transactions, OphthaliX raised approximately $3.33 million from a group of investors in a private placement of 646,776 shares of OphthaliX common stock, which represented approximately 6.2% of the issued and outstanding share capital of OphthaliX. As part of the private placement, Pnina Fishman, our Chief Executive Officer, invested $50,000 in OphthaliX and Guy Regev purchased shares of OphthaliX common stock from former OphthaliX shareholders for $75,000, each after approval by our audit committee and Board of Directors.

The acquisition transactions valued OphthaliX at approximately $50 million.

In connection with the acquisition transactions, we agreed not to withdraw any money from Eye-Fite or OphthaliX, except for the payments under the Services Agreement pursuant to which we are reimbursed for our costs plus 15%. See "—OphthaliX Agreements—Service Agreement".

For additional information with respect to the Spin-Off Agreements, see "—OphthaliX Agreements—Service Agreement" and "Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements—Eye-Fite Agreement".

Services Agreement

On November 21, 2011, we entered into a services agreement, or the Services Agreement, with OphthaliX and Eye-Fite, pursuant to which we provide management services to OphthaliX and Eye-Fite with respect to (i) all pre-clinical and clinical research studies of CF101 in the ophthalmic field, (ii) drug manufacturing and supply with respect to the compounds related to the Eye-Fite Agreement, (iii) QT studies in human beings, and (iv) payments to consultants that are listed in the Services Agreement for their involvement in the clinical trials and in all other activities necessary to launch CF101 for the treatment of ophthalmic diseases. As consideration for the foregoing services, we will be reimbursed by OphthaliX for our costs and expenses incurred in rendering such services plus 15% (not including VAT, if applicable) and in relation to expenses and costs of intellectual property maintenance, we will "pass through" any such payments and expenses made to third parties and will receive reimbursement for such costs and expenses from OphthaliX. In addition, OphthaliX must abide by all current ongoing clinical trial agreements that we are party to and OphthaliX must pay all payments under those agreements from November 21, 2011 onwards. Further, we are entitled to an additional payment of 2.5%, or the additional payment, of any revenues received by OphthaliX and Eye-Fite in connection with the use of CF101 in the ophthalmic field.

During the five-year period following the date of the execution of the Services Agreement, we are entitled to convert our right to the additional payment into a warrant to purchase 480,022 shares of OphthaliX common stock exercisable at $5.148 per share, representing approximately 5% of the shares of OphthaliX common stock on a fully diluted basis as of the date of closing of the Spin-Off Agreements and the Services Agreement. The Services Agreement is for an unlimited duration. However, following the first anniversary of the execution of the Services Agreement, each party is entitled to terminate the agreement if at least six months' prior notice, or less with respect to termination for "cause", as defined in the Services Agreement, is provided to the counterparty.

In February 2013, we sent a formal letter to OphthaliX, which has been updated periodically (most recently in March 2015), agreeing to defer payments owed to us under the Services Agreement beginning on January 31, 2013 for the performance of the clinical trials of CF101 in ophthalmic indications until the completion of fundraising by OphthaliX sufficient to cover such deferred payments. As of December 31, 2014, the deferred payments to Can-Fite totaled approximately $2,457,000. In addition, in March 2015, we issued a financial support letter pursuant to which we committed to cover any shortfall in OphthaliX's costs and expenses of the operations which are in excess of its available cash to finance its operations, including cash generated from any future sale of Can-Fite shares held by OphthaliX. Both letters remain in effect for a period of at least 14 months from March 2015 and any related balance bears interest at a rate of 3% per annum.

License Agreement

See "Item 4. Information on the Company—Business Overview—Out-Licensing and Distribution Agreements—Eye-Fite Agreement".

Employment and Consulting Agreements

See "Item 6. Directors, Senior Management and Employees—Compensation—Employment and Consulting Agreements".

D. Exchange Controls

There are no Israeli government laws, decrees or regulations that restrict or that affect our export or import of capital or the remittance of dividends, interest or other payments to non-resident holders of our securities, including the availability of cash and cash equivalents for use by us and our wholly-owned subsidiaries, except or otherwise as set forth under "Item 10.E. Additional Information — Taxation."

E. Taxation

Certain Israeli Tax Considerations

The following is a summary of the material Israeli tax laws applicable to us. This section also contains a discussion of material Israeli tax consequences concerning the ownership and disposition of our ordinary shares. This summary does not discuss all the aspects of Israeli tax law that may be relevant to a particular investor in light of his or her personal investment circumstances or to some types of investors subject to special treatment under Israeli law. Examples of this kind of investor include residents of Israel or traders in securities who are subject to special tax regimes not covered in this discussion. Because certain parts of this discussion are based on new tax legislation that has not yet been subject to judicial or administrative interpretation, we cannot assure you that the appropriate tax authorities or the courts will accept the views expressed in this discussion. The discussion does not cover all possible tax consequences.

You are urged to consult your own tax advisor as to the Israeli and other tax consequences of the purchase, ownership and disposition of our ADSs, including, in particular, the effect of any non-Israeli, state or local taxes.

General Corporate Tax Structure in Israel

Israeli companies are generally subject to a corporate tax at the rate of 25% of their taxable income in 2013 and thereafter. Capital gains derived by an Israeli company are generally subject to tax at a rate of 25%, or at the prevailing corporate tax rate, whichever is lower.

In 2006, transfer pricing regulations came into force, following the introduction of Section 85A of the Israeli Tax Ordinance under Amendment 132. The transfer pricing rules require that cross-border transactions between related parties be carried out implementing an arms' length principle and reported and taxed accordingly.

In 2008, the Knesset passed an amendment to the Income Tax (Inflationary Adjustments) Law, 1985, which limits the scope of the law starting in 2008 and thereafter. Starting in 2008, the revenues for tax purposes are measured in nominal values, excluding certain adjustments for changes in the consumer price index carried out in the period up to December 31, 2007. The amended law includes, among other provisions, the elimination of the inflationary additions and deductions and the additional deduction for depreciation for the period starting in 2008.

Pre-Ruling from the Israeli Income Tax Authorities

In connection with the Spin-Off, we received a pre-ruling decision from the Israeli Income Tax Authority which confirms: (i) that the grant of the license to Eye-Fite is not liable for tax pursuant to the provisions of section 104a to the Income Tax Ordinance (New Version), 1961, or the Ordinance; (ii) that OphthaliX is considered the receiving company pursuant to section 103c(7)(b) to the Ordinance; (iii) that the sale of Eye-Fite shares to OphthaliX as consideration for OphthaliX shares does not create liability for tax pursuant to the provisions of section 103t to the Ordinance, or change in structure; and (iv) the date for the change in structure was determined. According to the tax pre-ruling, the date of change in structure shall also be the date of exchange of shares with respect to the spin-off and notification to the tax assessor. We and Eye-Fite presented to the tax assessor and the merger and spin-off department of the tax assessor the forms required by the Ordinance and the regulations thereunder. The tax pre-ruling further provides that the grant of a license to Eye-Fite as consideration for the issuance of Eye-Fite shares to us does not create liability for tax pursuant to the provisions of section 104a to the Ordinance.

According to the pre-ruling, we must not sell more than 10% of our common stock holdings in OphthaliX issued in connection with the change in structure for at least two years from the date of the change (i.e., November 21, 2011), OphthaliX must not sell more than 10% of its ordinary share holdings in Eye-Fite received in connection with the change in structure for at least two years from the date of the change and Eye-Fite must retain the assets received from us in connection with the change in structure for at least two years from the date of the change.

The shares of Eye-Fite which were transferred to OphthaliX in connection with the change in structure will be held in escrow. The sale of these shares will be deemed as a sale by an Israeli company and will be taxed accordingly. The trustee will withhold tax at the source.

The shares of OphthaliX which were transferred to us in connection with the change in structure will be held in escrow. The sale of these shares will be deemed as a sale by an Israeli company and will be taxed accordingly. The trustee will withhold tax at the source.

Any dividend distributed by Eye-Fite to OphthaliX will be taxed in Israel in accordance with paragraph 125(b)5 of the Israeli Tax Ordinance.

A description of the terms of the pre-ruling is also included in the notes to the financial statements.

Tax Benefits and Grants for Research and Development

Israeli tax law allows, under certain conditions, a tax deduction for research and development expenditures, including capital expenditures, for the year in which they are incurred. These expenses must relate to scientific research and development projects and must be approved by the Office of the Chief Scientist, or the OCS, of the relevant Israeli government ministry, determined by the field of research. Furthermore, the research and development must be for the promotion of the company and carried out by or on behalf of the company seeking such tax deduction. The amount of such deductible expenses is reduced by the sum of any funds received through government grants for the funding of the scientific research and development projects. No deduction under these research and development deduction rules is allowed if such deduction is related to an expense invested in an asset depreciable under the general depreciation rules of the Tax Ordinance. Expenditures not so approved are deductible in equal amounts over three years.

On a yearly basis, we evaluate the applicability of the above tax deduction for research and development expenditures and, based on our evaluation, determine whether to apply to the OCS for approval of a tax deduction. There can be no assurance that any application for a tax deduction will be accepted.

Taxation of our Shareholders

Capital Gains Taxes Applicable to Non-Israeli Resident Shareholders. Shareholders that are not Israeli residents are generally exempt from Israeli capital gains tax on any gains derived from the sale, exchange or disposition of our shares, provided that such shareholders did not acquire their shares prior to our initial public offering on the TASE and such gains were not derived from a permanent establishment or business activity of such shareholders in Israel. However, non-Israeli corporations will not be entitled to the foregoing exemptions if an Israeli resident (i) has a controlling interest of 25% or more in such non-Israeli corporation or (ii) is the beneficiary of or is entitled to 25% or more of the revenues or profits of such non-Israeli corporation, whether directly or indirectly.

In addition, under the U.S.-Israel Income Tax Treaty, 1995, or the U.S.-Israel Tax Treaty, the sale, exchange or disposition of our shares by a shareholder who is a U.S. resident (for purposes of the U.S.-Israel Tax Treaty) holding the shares as a capital asset is exempt from Israeli capital gains tax unless either (i) the shareholder holds, directly or indirectly, shares representing 10% or more of our voting capital during any part of the 12-month period preceding such sale, exchange or disposition or (ii) the capital gains arising from such sale are attributable to a permanent establishment of the shareholder located in Israel. In either case, the sale, exchange or disposition of the shares would be subject to Israeli tax, to the extent applicable; however, under the U.S.-Israel Tax Treaty, the U.S. resident would be permitted to claim a credit for the tax against the U.S. federal income tax imposed with respect to the sale, exchange or disposition, subject to the limitations in U.S. laws applicable to foreign tax credits. The U.S.-Israel Tax Treaty does not relate to U.S. state or local taxes.

Shareholders may be required to demonstrate that they are exempt from tax on their capital gains in order to avoid withholding at source at the time of sale.

Taxation of Non-Israeli Shareholders on Receipt of Dividends. Non-residents of Israel are generally subject to Israeli income tax on the receipt of dividends paid on our shares at the rate of 20%, which tax will be withheld at the source, unless a different rate is provided in a tax treaty between Israel and the shareholder's country of residence. With respect to a person who is a "substantial shareholder" at the time receiving the dividend or on any date in the 12 months preceding such date, the applicable tax rate is 25%. A "substantial shareholder" is generally a person who alone, or together with his relative or another person who collaborates with him on a permanent basis, holds, directly or indirectly, at least 10% of any of the "means of control" of the corporation. "Means of control" generally include the right to vote, receive profits, nominate a director or an officer, receive assets upon liquidation, or order someone who holds any of the aforesaid rights how to act, and all regardless of the source of such right. Under the U.S.-Israel Tax Treaty, the maximum rate of tax withheld in Israel on dividends paid to a holder of our ordinary shares who is a U.S. resident (for purposes of the U.S.-Israel Tax Treaty) is 25%. However, generally, the maximum rate of withholding tax on dividends that are paid to a U.S. corporation holding 10% or more of our outstanding voting capital throughout the tax year in which the dividend is distributed as well as the previous tax year is 12.5%.

A non-resident of Israel who receives dividends from which tax was withheld is generally exempt from the duty to file returns in Israel in respect of such income, provided such income was not derived from a business conducted in Israel by the taxpayer, and the taxpayer has no other taxable sources of income in Israel.

Taxation of Israeli Shareholders on Receipt of Dividends

Residents of Israel are generally subject to Israeli income tax on the receipt of dividends paid on our shares at the rate of 25%, which tax will be withheld at the source. With respect to a person who is a "substantial shareholder" at the time of receiving the dividend or on any date within the 12 months preceding such date, the applicable tax rate is 30%.

U.S. Federal Income Tax Consequences

The following is a general summary of what we believe to be material U.S. federal income tax consequences relating to the purchase, ownership and disposition of our ordinary shares and ADSs by U.S. Investors (as defined below) that hold such shares or ADSs as capital assets. This summary is based on the Internal Revenue Code, or the Code, the regulations of the U.S. Department of the Treasury issued pursuant to the Code, or the Treasury Regulations, and administrative and judicial interpretations thereof, all as in effect on the date hereof and all of which are subject to change, possibly with retroactive effect, or to different interpretation. No ruling has been sought from the IRS with respect to any United States federal income tax consequences described below, and there can be no assurance that the IRS or a court will not take a contrary position. This summary does not address all of the tax considerations that may be relevant to specific U.S. Investors in light of their particular circumstances or to U.S. Investors subject to special treatment under U.S. federal income tax law (such as banks, insurance companies, tax-exempt entities, retirement plans, regulated investment companies, partnerships, dealers in securities, brokers, real estate investment trusts, certain former citizens or residents of the United States, persons who acquire our shares or ADSs as part of a straddle, hedge, conversion transaction or other integrated investment, persons that have a "functional currency" other than the U.S. dollar, persons that own (or are deemed to own, indirectly or by attribution) 10% or more of our shares or ADSs or persons that generally mark their securities to market for U.S. federal income tax purposes). This summary does not address any U.S. state or local or non-U.S. tax considerations or any U.S. federal estate, gift or alternative minimum tax considerations or any U.S. federal tax consequences other than U.S. federal income tax consequences.

As used in this summary, the term "U.S. Investor" means a beneficial owner of our shares or ADSs that is, for U.S. federal income tax purposes, (i) an individual citizen or resident of the United States, (ii) a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, (iii) an estate the income of which is subject to U.S. federal income tax regardless of its source or (iv) a trust with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions, or that has a valid election in effect under applicable Treasury Regulations to be treated as a "United States person."

If an entity treated as a partnership for U.S. federal income tax purposes holds our shares or ADSs, the tax treatment of such partnership and each partner thereof will generally depend upon the status and activities of the partnership and such partner. A holder that is treated as a partnership for U.S. federal income tax purposes should consult its own tax advisor regarding the U.S. federal income tax considerations applicable to it and its partners of the purchase, ownership and disposition of its shares or ADSs.

Prospective investors should be aware that this summary does not address the tax consequences to investors who are not U.S. Investors. Prospective investors should consult their own tax advisors as to the particular tax considerations applicable to them relating to the purchase, ownership and disposition of their shares or ADSs, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

Taxation of U.S. Investors

The discussions under "— Distributions" and under "— Sale, Exchange or Other Disposition of Ordinary Shares and ADSs" below assumes that we will not be treated as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. We believe that we may be a PFIC during 2014 although we have not determined whether we will be a PFIC in 2015, or in any subsequent year,our operating results for any such years may cause us to be a PFIC.For a discussion of the rules that would apply if we are treated as a PFIC, see the discussion under "— Passive Foreign Investment Company."

Distributions. We have no current plans to pay dividends. To the extent we pay any dividends, a U.S. Investor will be required to include in gross income as a taxable dividend the amount of any distributions made on the shares or ADSs, including the amount of any Israeli taxes withheld, to the extent that those distributions are paid out of our current or accumulated earnings and profits as determined for U.S. federal income tax purposes. Any distributions in excess of our earnings and profits will be applied against and will reduce the U.S. Investor's tax basis in its shares or ADSs and to the extent they exceed that tax basis, will be treated as gain from the sale or exchange of those shares or ADSs. If we were to pay dividends, we expect to pay such dividends in NIS with respect to the shares and in U.S. dollars with respect to ADSs. A dividend paid in NIS, including the amount of any Israeli taxes withheld, will be includible in a U.S. Investor's income as a U.S. dollar amount calculated by reference to the exchange rate in effect on the date such dividend is received, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted to U.S. dollars on the date of receipt, a U.S. Investor generally will not recognize a foreign currency gain or loss. However, if the U.S. Investor converts the NIS into U.S. dollars on a later date, the U.S. Investor must include, in computing its income, any gain or loss resulting from any exchange rate fluctuations. The gain or loss will be equal to the difference between (i) the U.S. dollar value of the amount included in income when the dividend was received and (ii) the amount received on the conversion of the NIS into U.S. dollars. Such gain or loss will generally be ordinary income or loss and United States source for U.S. foreign tax credit purposes. U.S. Investors should consult their own tax advisors regarding the tax consequences to them if we pay dividends in NIS or any other non-U.S. currency.

Subject to certain significant conditions and limitations, including potential limitations under the U.S.-Israel Tax Treaty, any Israeli taxes paid on or withheld from distributions from us and not refundable to a U.S. Investor may be credited against the investor's U.S. federal income tax liability or, alternatively, may be deducted from the investor's taxable income. This election is made on a year-by-year basis and applies to all foreign taxes paid by a U.S. Investor or withheld from a U.S. Investor that year. Dividends paid on the shares generally will constitute income from sources outside the United States and be categorized as "passive category income" or, in the case of some U.S. Investors, as "general category income" for U.S. foreign tax credit purposes.

Because the rules governing foreign tax credits are complex, U.S. Investors should consult their own tax advisor regarding the availability of foreign tax credits in their particular circumstances. In addition, the U.S. Treasury Department has expressed concerns that parties to whom ADSs are pre-released may be taking actions that are inconsistent with the claiming of foreign tax credits by U.S. holders of ADSs. Accordingly, the creditability of Israeli taxes could be affected by future actions that may be taken by the U.S. Treasury Department or parties to whom ADSs are pre-released.

Dividends paid on the shares and ADSs will not be eligible for the "dividends-received" deduction generally allowed to corporate U.S. Investors with respect to dividends received from U.S. corporations.

For taxable years beginning after December 31, 2012, certain distributions treated as dividends that are received by an individual U.S. Investor from "qualified foreign corporations" generally qualify for a 20% reduced maximum tax rate so long as certain holding period and other requirements are met. A non-US. corporation (other than a corporation that is treated as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (i) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information program, or (ii) with respect to any dividend it pays on stock (or ADSs in respect of such stock) which is readily tradable on an established securities market in the United States. Dividends paid by us in a taxable year in which we are not a PFIC and with respect to which we were not a PFIC in the preceding taxable year are expected to be eligible for the 20% reduced maximum tax rate, although we can offer no assurances in this regard. However, any dividend paid by us in a taxable year in which we are a PFIC or were a PFIC in the preceding taxable year will be subject to tax at regular ordinary income rates. As mentioned above, we have not determined whether we are currently a PFIC or not.

Sale, Exchange or Other Disposition of Ordinary Shares and ADSs. Subject to the discussion under "— Passive Foreign Investment Company" below, a U.S. Investor generally will recognize capital gain or loss upon the sale, exchange or other disposition of our shares or ADSs in an amount equal to the difference between the amount realized on the sale, exchange or other disposition and the U.S. Investor's adjusted tax basis in such shares. This capital gain or loss will be long-term capital gain or loss if the U.S. Investor's holding period in our shares exceeds one year. Preferential tax rates for long-term capital gain (currently, with a maximum rate of 20% for taxable years beginning after December 31, 2012) will apply to individual U.S. Investors. The deductibility of capital losses is subject to limitations. The gain or loss will generally be income or loss from sources within the United States for U.S. foreign tax credit purposes, subject to certain exceptions in U.S.-Israel Tax Treaty.

U.S. Investors should consult their own tax advisors regarding the U.S. federal income tax consequences of receiving currency other than U.S. dollars upon the disposition of their shares or ADSs.

Passive Foreign Investment Company

In general, a corporation organized outside the United States will be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of its gross income is "passive income" or (ii) on average at least 50% of its assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in the public offering. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Under the tests described above, whether or not we are a PFIC will be determined annually based upon the composition of our income and the composition and valuation of our assets, all of which are subject to change.

We believe that we may be a PFIC during 2014 although we have not determined whether we will be a PFIC in 2015, or in any subsequent year,our operating results for any such years may cause us to be a PFIC.

U.S. Investors should be aware of certain tax consequences of investing directly or indirectly in us if we are a PFIC. A U.S. Investor is subject to different rules depending on whether the U.S. Investor makes an election to treat us as a "qualified electing fund," known as a QEF election, for the first taxable year that the U.S. Investor holds shares or ADSs, which is referred to in this disclosure as a "timely QEF election," makes a "mark-to-market" election with respect to the shares or ADSs (if such election is available), or makes neither election.

QEF Election. A U.S. Investor who makes a timely QEF election, referred to in this disclosure as an "Electing U.S. Investor," with respect to us must report for U.S. federal income tax purposes his pro rata share of our ordinary earnings and net capital gain, if any, for our taxable year that ends with or within the taxable year of the Electing U.S. Investor. The "net capital gain" of a PFIC is the excess, if any, of the PFIC's net long-term capital gains over its net short-term capital losses. The amount so included in income generally will be treated as ordinary income to the extent of such Electing U.S. Investor's allocable share of the PFIC's ordinary earnings and as long-term capital gain to the extent of such Electing U.S. Investor's allocable share of the PFIC's net capital gains. Such Electing U.S. Investor generally will be required to translate such income into U.S. dollars based on the average exchange rate for the PFIC's taxable year with respect to the PFIC's functional currency. Such income generally will be treated as income from sources outside the United States for U.S. foreign tax credit purposes. Amounts previously included in income by such Electing U.S. Investor under the QEF rules generally will not be subject to tax when they are distributed to such Electing U.S. Investor. The Electing U.S. Investor's tax basis in our shares or ADSs generally will increase by any amounts so included under the QEF rules and decrease by any amounts not included in income when distributed.

An Electing U.S. Investor will be subject to U.S. federal income tax on such amounts for each taxable year in which we are a PFIC, regardless of whether such amounts are actually distributed to such Electing U.S. Investor. However, an Electing U.S. Investor may, subject to certain limitations, elect to defer payment of current U.S. federal income tax on such amounts, subject to an interest charge. If an Electing U.S. Investor is an individual, any such interest will be treated as non-deductible "personal interest."

Any net operating losses or net capital losses of a PFIC will not pass through to the Electing U.S. Investor and will not offset any ordinary earnings or net capital gain of a PFIC recognized by Electing U.S. Investors in subsequent years.

So long as an Electing U.S. Investor's QEF election with respect to us is in effect with respect to the entire holding period for our shares or ADSs, any gain or loss recognized by such Electing U.S. Investor on the sale, exchange or other disposition of such shares or ADSs generally will be long-term capital gain or loss if such Electing U.S. Investor has held such shares or ADSs for more than one year at the time of such sale, exchange or other disposition. Preferential tax rates for long-term capital gain (currently, a maximum rate of 20% for taxable years beginning after December 31, 2012) will apply to individual U.S. Investors. The deductibility of capital losses is subject to limitations.

In general, a U.S. Investor must make a QEF election on or before the due date for filing its income tax return for the first year to which the QEF election is to apply. A U.S. Investor makes a QEF election by completing the relevant portions of and filing IRS Form 8621 in accordance with the instructions thereto. Upon request, we will annually furnish U.S. Investors with information needed in order to complete IRS Form 8621 (which form would be required to be filed with the IRS on an annual basis by the U.S. Investor) and to make and maintain a valid QEF election for any year in which we or any of our subsidiaries that we control is a PFIC. There is no assurance, however, that we will have timely knowledge of our status as a PFIC, or that the information that we provide will be adequate to allow U.S. Investors to make a QEF election. A QEF election will not apply to any taxable year during which we are not a PFIC, but will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Each U.S. Investor should consult its own tax advisor with respect to the advisability of, the tax consequences of, and the procedures for making a QEF election with respect to us.

Mark-to-Market Election. Alternatively, if our shares or ADSs are treated as "marketable stock," a U.S. Investor would be allowed to make a "mark-to-market" election with respect to our shares or ADSs, provided the U.S. Investor completes and files IRS Form 8621 in accordance with the relevant instructions and related Treasury Regulations. If that election is made, the U.S. Investor generally would include as ordinary income in each taxable year the excess, if any, of the fair market value of our shares or ADSs at the end of the taxable year over such holder's adjusted tax basis in such shares or ADSs. The U.S. Investor would also be permitted an ordinary loss in respect of the excess, if any, of the U.S. Investor's adjusted tax basis in our shares or ADSs over their fair market value at the end of the taxable year, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. A U.S. Investor's tax basis in our shares or ADSs would be adjusted to reflect any such income or loss amount. Gain realized on the sale, exchange or other disposition of our shares or ADSs would be treated as ordinary income, and any loss realized on the sale, exchange or other disposition of our shares or ADSs would be treated as ordinary loss to the extent that such loss does not exceed the net mark-to-market gains previously included in income by the U.S. Investor, and any loss in excess of such amount will be treated as capital loss. Amounts treated as ordinary income will not be eligible for the favorable tax rates applicable to qualified dividend income or long-term capital gains.

Generally, stock will be considered marketable stock if it is "regularly traded" on a "qualified exchange" within the meaning of applicable Treasury Regulations. A class of stock is regularly traded on an exchange during any calendar year during which such class of stock is traded, other than in *de minimis* quantities, on at least 15 days during each calendar quarter. To be marketable stock, our shares and ADSs must be regularly traded on a qualifying exchange (i) in the United States that is registered with the SEC or a national market system established pursuant to the Exchange Act. or (ii) outside the United States that is properly regulated and meets certain trading, listing, financial disclosure and other requirements. Our shares should constitute "marketable stock" as long as they remain listed on the OTC and/or the NYSE MKT and are regularly traded. Our ADSs will be listed on the OTC and/or the NYSE MKT. While we believe that our ADSs may be treated as marketable stock for purposes of the PFIC rules so long as they are listed on the OTC and/or the NYSE MKT and are regularly traded, the IRS has not provided a list of the exchanges that meet the foregoing requirements and thus no assurance can be provided that our ADSs will be (or will remain) treated as marketable stock for purposes of the PFIC rules.

A mark-to-market election will not apply to our shares or ADSs held by a U.S. Investor for any taxable year during which we are not a PFIC, but will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Such election will not apply to any PFIC subsidiary that we own. Each U.S. Investor is encouraged to consult its own tax advisor with respect to the availability and tax consequences of a mark-to-market election with respect to our shares and ADSs.

Default PFIC Rules. A U.S. Investor who does not make a timely QEF election or a mark-to-market election, referred to in this disclosure as a "Non-Electing U.S. Investor," will be subject to special rules with respect to (i) any "excess distribution" (generally, the portion of any distributions received by the Non-Electing U.S. Investor on the shares or ADSs in a taxable year in excess of 125% of the average annual distributions received by the Non-Electing U.S. Investor in the three preceding taxable years, or, if shorter, the Non-Electing U.S. Investor's holding period for the shares or ADSs), and (ii) any gain realized on the sale or other disposition of such shares or ADSs. Under these rules:

- the excess distribution or gain would be allocated ratably over the Non-Electing U.S. Investor's holding period for such shares or ADSs;
- the amount allocated to the current taxable year and any year prior to us becoming a PFIC would be taxed as ordinary income; and
- the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year.

If a Non-Electing U.S. Investor who is an individual dies while owning our shares or ADSs, the Non-Electing U.S. Investor's successor would be ineligible to receive a step-up in tax basis of such shares or ADSs. Non-Electing U.S. Investors should consult their tax advisors regarding the application of the PFIC rules to their specific situation.

A Non-Electing U.S. Investor who wishes to make a QEF election for a subsequent year may be able to make a special "purging election" pursuant to Section 1291(d) of the Code. Pursuant to this election, a Non-Electing U.S. Investor would be treated as selling his or her shares or ADSs for fair market value on the first day of the taxable year for which the QEF election is made. Any gain on such deemed sale would be subject to tax under the rules for Non-Electing U.S. Investors as discussed above. Non-Electing U.S. Investors should consult their tax advisors regarding the availability of a "purging election" as well as other available elections.

To the extent a distribution on our shares or ADSs does not constitute an excess distribution to a Non-Electing U.S. Investor, such Non-Electing U.S. Investor generally will be required to include the amount of such distribution in gross income as a dividend to the extent of our current or accumulated earnings and profits (as determined for U.S. federal income tax purposes) that are not allocated to excess distributions. The tax consequences of such distributions are discussed above under "— Taxation of U.S. Investors — Distributions." Each U.S. Holder is encouraged to consult its own tax advisor with respect to the appropriate U.S. federal income tax treatment of any distribution on our shares.

If we are treated as a PFIC for any taxable year during the holding period of a Non-Electing U.S. Investor, we will continue to be treated as a PFIC for all succeeding years during which the Non-Electing U.S. Investor is treated as a direct or indirect Non-Electing U.S. Investor even if we are not a PFIC for such years. A U.S. Investor is encouraged to consult its tax advisor with respect to any available elections that may be applicable in such a situation, including the "deemed sale" election of Code Section 1298(b)(1) (which will be taxed under the adverse tax rules described above). In addition, U.S. Investors should consult their tax advisors regarding the IRS information reporting and filing obligations that may arise as a result of the ownership of shares in a PFIC.

We may invest in the equity of foreign corporations that are PFICs or may own subsidiaries that own PFICs. If we are classified as a PFIC, under attribution rules U.S. Investors will be subject to the PFIC rules with respect to their indirect ownership interests in such PFICs, such that a disposition of the shares of the PFIC or receipt by us of a distribution from the PFIC generally will be treated as a deemed disposition of such shares or the deemed receipt of such distribution by the U.S. Investor, subject to taxation under the PFIC rules. There can be no assurance that a U.S. Investor will be able to make a QEF election or a mark-to-market election with respect to PFICs in which we invest. Each U.S. Investor is encouraged to consult its own tax advisor with respect to tax consequences of an investment by us in a corporation that is a PFIC.

The U.S. federal income tax rules relating to PFICs, QEF elections, and mark-to market elections are complex. U.S. Investors are urged to consult their own tax advisors with respect to the purchase, ownership and disposition of our shares or ADSs, any elections available with respect to such shares or ADSs and the IRS information reporting obligations with respect to the purchase, ownership and disposition of our shares or ADSs.

Certain Reporting Requirements

Certain U.S. Investors are required to file IRS Form 926, Return by U.S. Transferor of Property to a Foreign Corporation, and certain U.S. Investors may be required to file IRS Form 5471, Information Return of U.S. Persons With Respect to Certain Foreign Corporations, reporting transfers of cash or other property to us and information relating to the U.S. Investor and us. Substantial penalties may be imposed upon a U.S. Investor that fails to comply.

In addition, recently enacted legislation requires certain U.S. Investors to report information on IRS Form 8938 with respect to their investments in certain "foreign financial assets," which under certain circumstances would include an investment in our shares and ADSs, to the IRS.

Investors who fail to report required information could become subject to substantial penalties. U.S. Investors should consult their tax advisors regarding the possible implications of these reporting requirements on their investment in our shares and ADSs.

Backup Withholding Tax and Information Reporting Requirements

Generally, information reporting requirements will apply to distributions on our shares or ADSs or proceeds on the disposition of our shares or ADSs paid within the United States (and, in certain cases, outside the United States) to U.S. Investors other than certain exempt recipients, such as corporations. Furthermore, backup withholding (currently at 28%) may apply to such amounts if the U.S. Investor fails to (i) provide a correct taxpayer identification number, (ii) report interest and dividends required to be shown on its U.S. federal income tax return, or (iii) make other appropriate certifications in the required manner. U.S. Investors who are required to establish their exempt status generally must provide such certification on IRS Form W-9.

Backup withholding is not an additional tax. Amounts withheld as backup withholding from a payment may be credited against a U.S. Investor's U.S. federal income tax liability and such U.S. Investor may obtain a refund of any excess amounts withheld by filing the appropriate claim for refund with the IRS and furnishing any required information in a timely manner.

New Legislative Developments

With respect to taxable years beginning after December 31, 2012, certain U.S. persons, including individuals, estates and trusts, will be subject to an additional 3.8% Medicare tax on unearned income. For individuals, the additional Medicare tax applies to the lesser of (i) "net investment income" or (ii) the excess of "modified adjusted gross income" over $200,000 ($250,000 if married and filing jointly or $125,000 if married and filing separately). "Net investment income" generally equals the taxpayer's gross investment income reduced by the deductions that are allocable to such income. Investment income generally includes passive income such as interest, dividends, annuities, royalties, rents, and capital gains. U.S. Investors are urged to consult their own tax advisors regarding the implications of the additional Medicare tax resulting from their ownership and disposition of our shares or ADSs.

U.S. Investors should consult their own tax advisors concerning the tax consequences relating to the purchase, ownership and disposition of our shares or ADSs.

F. Dividends and Paying Agents.

Not applicable.

G. Statements by Experts.

Not applicable.

H. Documents on Display.

We are subject to the information reporting requirements of the Exchange Act, applicable to foreign private issuers and under those requirements will file reports with the SEC. Those other reports or other information and this Annual Report may be inspected without charge at 10 Bareket Street, Kiryat Matalon, Petah-Tikva 4951778, Israel, and inspected and copied at the public reference facilities of the SEC located at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC also maintains a website at *http://www.sec.gov* from which certain filings may be accessed.

As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act. However, we will file with the SEC, within 120 days after the end of each fiscal year, or such applicable time as required by the SEC, an annual report on Form 20-F containing financial statements audited by an independent registered public accounting firm, and will submit to the SEC, on a Form 6-K, unaudited quarterly financial information.

In addition, because our ordinary shares are traded on the TASE, we have filed Hebrew language periodic and immediate reports with, and furnish information to, the TASE and the ISA, as required under Chapter Six of the Israel Securities Law. Copies of our filings with the ISA can be retrieved electronically through the MAGNA distribution site of the ISA (*www.magna.isa.gov.il*) and the TASE website (*www.maya.tase.co.il*).

We maintain a corporate website at *www.canfite.com*. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report on Form 20-F. We have included our website address in this Annual Report on Form 20-F solely as an inactive textual reference.

I. Subsidiary Information.

Not applicable.

ITEM 11. Quantitative and Qualitative Disclosures About Market Risk

Market risk is the risk of loss related to changes in market prices, including interest rates and foreign exchange rates, of financial instruments that may adversely impact our consolidated financial position, results of operations or cash flows.

Interest Rate Risk

We do not anticipate undertaking any significant long-term borrowings. At present, our investments consist primarily of cash and cash equivalents. We may invest in investment-grade marketable securities with maturities of up to three years, including commercial paper, money market funds, and government/non-government debt securities. The primary objective of our investment activities is to preserve principal while maximizing the income that we receive from our investments without significantly increasing risk and loss. Our investments are exposed to market risk due to fluctuation in interest rates, which may affect our interest income and the fair market value of our investments, if any. We manage this exposure by performing ongoing evaluations of our investments. Due to the short-term maturities, if any, of our investments to date, their carrying value has always approximated their fair value. If we decide to invest in investments other than cash and cash equivalents, it will be our policy to hold such investments to maturity in order to limit our exposure to interest rate fluctuations.

Foreign Currency Exchange Risk

Our foreign currency exposures give rise to market risk associated with exchange rate movements of the NIS, our functional and reporting currency, mainly against the dollar and the euro. Although the NIS is our functional currency, a significant portion of our expenses are denominated in both dollars and Euros and currently all of our revenues are denominated in dollars. Our U.S. dollar and euro expenses consist principally of payments made to sub-contractors and consultants for preclinical studies, clinical trials and other research and development activities. We anticipate that a sizable portion of our expenses will continue to be denominated in currencies other than the NIS. If the NIS fluctuates significantly against either the U.S. dollar or the euro, it may have a negative impact on our results of operations. To date, fluctuations in the exchange rates have not materially affected our results of operations or financial condition for the periods under review.

To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations.

ITEM 12. Description of Securities Other Than Equity Securities

A. Debt Securities.

Not applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares

The Bank of New York Mellon, as Depositary, has registered and delivered American Depositary Shares, or ADSs. Each ADS represents two (2) ordinary shares (or a right to receive two (2) ordinary shares) deposited with the principal Tel Aviv office of Bank Hapoalim, as custodian for the Depositary. Each ADS also represents any other securities, cash or other property which may be held by the Depositary. The Depositary's corporate trust office at which the ADSs are administered is located at 101 Barclay Street, New York, New York 10286. The Bank of New York Mellon's principal executive office is located at One Wall Street, New York, New York 10286.

The form of the deposit agreement for the ADSs and the form of American Depositary Receipt that represents an ADS have been incorporated by reference as exhibits to this Annual Report on Form 20-F.

Fees and Expenses

***Persons depositing or withdrawing shares or ADS holders must pay*:**	***For*:**
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	● Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property ● Cancellation of ADSs for the purpose of withdrawal, including if the Deposit Agreement terminates
$.05 (or less) per ADS	● Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	● Distribution of securities distributed to holders of deposited securities which are distributed by the Depositary to ADS holders
$.05 (or less) per ADSs per calendar year	● Depositary services
Registration or transfer fees	● Transfer and registration of shares on our share register to or from the name of the Depositary or its agent when you deposit or withdraw shares
Expenses of the Depositary	● Cable, telex and facsimile transmissions (when expressly provided in the Deposit Agreement) ● Converting foreign currency to U.S. dollars
Taxes and other governmental charges the Depositary or the custodian have to pay on any ADS or share underlying an ADS, for example, stock transfer taxes, stamp duty or withholding taxes	● As necessary
Any charges incurred by the Depositary or its agents for servicing the deposited securities	● As necessary

The Depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The Depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The Depositary may collect its annual fee for depositary services by deduction from cash distributions, by directly billing investors or by charging the book-entry system accounts of participants acting for them. The Depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the Depositary may make payments to us to reimburse us for expenses and/or share revenue with us from the fees collected from ADS holders, or waive fees and expenses for services provided, generally relating to costs and expenses arising out of the establishment and maintenance of the ADS program. In performing its duties under the Deposit Agreement, the Depositary may use brokers, dealers or other service providers that are affiliates of the Depositary and that may earn or share fees or commissions.

PART II

ITEM 13. Defaults, Dividend Arrearages and Delinquencies

Not applicable.

ITEM 14. Material Modifications to the Rights of Security Holders and Use of Proceeds

Registered Direct Offering

The effective date of the registration statement, File No. 333-199033, on Form F-3 was October 21, 2014. In an at-the-market registered direct offering that closed on December 8, 2014, we sold an aggregate of 1,797,753 ADSs at $4.45 per share for aggregate gross proceeds of $8,000,000. In addition, the investors received unregistered warrants to purchase 898,877 ADSs. The warrants may be exercised at any time for a period of five years from issuance and have an exercise price of $4.45 per ADS, subject to adjustment as set forth therein. The warrants may be exercised on a cashless basis if six months after issuance there is no effective registration statement registering the ADSs underlying the warrants.

H.C. Wainwright & Co., LLC acted as placement agent and Roth Capital Partners LLC acted as a financial advisor in connection with the offering.

The total expenses of the offering, including placement agent fees were approximately $0.8 million. The net proceeds that we received from the offering were approximately $7.2 million.

From the closing until December 31, 2014, we have used existing cash and the net proceeds from the offering, in the amount of approximately $0.6 million for working capital and other general corporate purposes. The balance is held in cash and cash equivalents.

None of the net proceeds of the offering was paid directly or indirectly to any director, officer, general partner of ours or to their associates, persons owning ten percent or more of any class of our equity securities, or to any of our affiliates, except as employee/consultant compensation and general and administrative expenses.

ITEM 15. Controls and Procedures

Disclosure controls and procedures

Our management, including our chief executive officer, or CEO, and our chief financial officer, or CFO, are responsible for establishing and maintaining our disclosure controls and procedures (within the meaning of Rule 13a-15(e) of the Exchange Act). These controls and procedures were designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC and that such information is accumulated and communicated to our management, including our CEO and CFO, as appropriate, to allow timely decisions regarding required disclosure. We evaluated these disclosure controls and procedures under the supervision of our CEO and CFO as of December 31, 2014. Based upon that evaluation, our management, including our CEO and CFO, concluded that our disclosure controls and procedures as of December 31, 2014 were effective.

Management's annual report on internal control over financial reporting

Our management, including our CEO, and our CFO, are responsible for establishing and maintaining adequate internal control over our financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act of 1934, as amended. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Internal control over financial reporting includes policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect our transactions and asset dispositions;
- provide reasonable assurance that transactions are recorded as necessary to permit the preparation of our financial statements in accordance with generally accepted accounting principles;
- provide reasonable assurance that receipts and expenditures are made only in accordance with authorizations of our management and board of directors (as appropriate); and
- provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Due to its inherent limitations, internal controls over financial reporting may not prevent or detect misstatements. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our CEO, and our CFO, we assessed the effectiveness of our internal control over financial reporting as of December 31, 2014 based on the framework for Internal Control-Integrated Framework set forth by The Committee of Sponsoring Organizations of the Treadway Commission (COSO)(2013).

Based on our assessment and this framework, our management concluded that our internal control over financial reporting were effective as of December 31, 2014

Attestation Report of Registered Public Accounting Firm

Not applicable.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting, other than as described above, that occurred during the year ended December 31, 2014 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. Audit Committee Financial Expert

Our Board of Directors has determined that Gil Oren is an audit committee financial expert, as defined by applicable SEC regulations. Gil Oren qualified as an "independent director," as that term is defined under NYSE MKT rules.

ITEM 16B. Code of Ethics

We have adopted a code of ethics, referred to as a Code of Business Conduct, applicable to our directors, officers and all other employees. Our code of ethics is publicly available on our website at www.canfite.com. If we make any amendment to the code of ethics or grant any waivers, including any implicit waiver, from a provision of the code of ethics, which applies to our chief executive officer, chief financial officer, chief accounting officer or controller, or persons performing similar functions, we will disclose the nature of such amendment or waiver on our website.

ITEM 16C. Principal Accountant Fees and Services

The following table sets forth, for each of the years indicated, the fees billed by our independent registered public accounting firm.

	Year Ended December 31,	
	2013	2014
Services Rendered	(in thousands of NIS)	
Audit (1)	370	370
Audit related services	-	29
Tax	-	-
All Other fees	-	-
Total	370	399

(1) Audit fees consist of services that would normally be provided in connection with statutory and regulatory filings or engagements, including services that generally only the independent accountant can reasonably provide.

Audit Committee Pre-Approval Policies and Procedures

Our audit committee's specific responsibilities in carrying out its oversight of the quality and integrity of the accounting, auditing and reporting practices of us include the approval of audit and non-audit services to be provided by the external auditor. The audit committee approves in advance the particular services or categories of services to be provided to us during the following yearly period and also sets forth a specific budget for such audit and non-audit services. Additional non-audit services may be pre-approved by the audit committee.

ITEM 16D. Exemptions from the Listing Standards for Audit Committees

Not applicable.

ITEM 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers

Not applicable.

ITEM 16F. Change in Registrant's Certifying Accountant

Not applicable.

ITEM 16G. Corporate Governance

We are a foreign private issuer whose ordinary shares are listed on the NYSE MKT. As such, we are required to comply with U.S. federal securities laws, including the Sarbanes-Oxley Act, and the NYSE MKT rules, including the NYSE MKT corporate governance requirements. The NYSE MKT rules provide that foreign private issuers may follow home country practice in lieu of certain qualitative listing requirements subject to certain exceptions and except to the extent that such exemptions would be contrary to U.S. federal securities laws, so long as the foreign issuer discloses that it does not follow such listing requirement and describes the home country practice followed in its reports filed with the SEC. Below is a concise summary of the significant ways in which our corporate governance practices differ from the corporate governance requirements of NYSE MKT applicable to domestic U.S. listed companies:

- The NYSE MKT rules recommend that an issuer have a quorum requirement for shareholders meetings of at least one-third of the outstanding shares of the issuer's common voting stock. We have chosen to follow home country practice with respect to the quorum requirements of our shareholders meeting and our adjourned shareholders meeting. Our articles of association, as permitted under the Israeli Companies Law and Israeli practice, provide that the quorum requirements for a shareholders meeting are the presence of at least two shareholders who represent at least 25%of the outstanding shares of the issuer's common voting stock, and in the event of an adjourned meeting, the presence of a minimum of two shareholders present in person.

- We have chosen to follow our home country practice in lieu of the requirements of the NYSE MKT rules relating to an issuer's furnishing of its annual report to shareholders. However, we post our Annual Report on Form 20-F on our web site (www.canfite.com) as soon as practicable following the filing of the Annual Report on Form 20-F with the SEC.

- We have chosen to follow our home country practice in lieu of the requirements of the NYSE MKT rules relating to shareholder approval required prior to the issuance of securities (i) when a stock option or purchase plan is to be established or materially amended or other equity compensation arrangement made or materially amended, pursuant to which stock may be acquired by any of controlling shareholders, our directors or the Chief Executive Officer and (ii) in connection with a transaction, other than a public offering, involving the issuance or potential issuance by the Company of common stock equal to 20% or more of the common stock or 20% or more of the voting power outstanding before the issuance, in any consecutive 12 months period. We follow the provisions of the Israeli Companies Law with regard to transactions with our affiliates, i.e., our controlling shareholder and our directors and officers, including private placement transactions.

ITEM 16H. Mine Safety Disclosure

Not applicable.

PART III

ITEM 17. Financial Statements

We have responded to Item 18 in lieu of responding to this item.

ITEM 18. Financial Statements

Please refer to the financial statements beginning on page F-1.

The following financial statements and financial statement schedules are filed as part of this Annual Report on Form 20-F, together with the report of the independent registered public accounting firm.

CAN-FITE BIOPHARMA LTD. AND ITS SUBSIDIARIES

CONSOLIDATED FINANCIAL STATEMENTS

AS OF DECEMBER 31, 2014

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors of

CAN-FITE BIOPHARMA LTD. AND ITS SUBSIDIARIES

We have audited the accompanying consolidated statements of financial position of Can-Fite Biopharma Ltd. and its subsidiaries (the "Company") as of December 31, 2014 and 2013, and the related consolidated statements of comprehensive loss, changes in equity and cash flows for each of the three years in the period ended December 31, 2014. These consolidated financial statements are the responsibility of the Company's board of directors and management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's and its subsidiaries internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances but not for the purpose of expressing an opinion on the effectiveness of the Company's and its subsidiaries internal control over financial reporting. Accordingly, we express no such opinion. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, based on our audits, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of the Company as of December 31, 2014 and 2013, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

/s/ Kost Forer Gabbay & Kasierer
KOST FORER GABBAY & KASIERER
A Member of Ernst & Young Global

Tel-Aviv, Israel
March 27, 2015

CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
In thousands (except for share and per share data)

	Note	December 31, 2014 USD Note 2.c.2	December 31, 2014 NIS	December 31, 2013 NIS
ASSETS				
CURRENT ASSETS:				
Cash and cash equivalents		9,280	36,091	20,767
Accounts receivable and prepaid expenses	6	879	3,417	2,161
Total current assets		10,159	39,508	22,928
NON-CURRENT ASSETS:				
Lease deposit		7	26	34
Property, plant and equipment, net	7	34	133	143
Total long-term assets		41	159	177
Total assets		10,200	39,667	23,105

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF FINANCIAL POSITION

In thousands (except for share and per share data)

	Note	December 31, 2014 USD Note 2.c.2	December 31, 2014 NIS	December 31, 2013 NIS
LIABILITIES AND SHAREHOLDERS' EQUITY				
CURRENT LIABILITIES:				
Trade payables	8	264	1,024	2,056
Other accounts payable	9	1,221	4,750	5,276
Warrants exercisable into shares (Series 7)	14	-	-	119
Total current liabilities		1,485	5,774	7,451
NON-CURRENT LIABILITIES:				
Warrants exercisable into shares	14	1,792	6,969	-
Severance pay, net	11	58	224	129
Total Long-term liabilities		1,850	7,193	129
CONTIGENT LIABILITIES AND COMMITMENTS	12			
EQUITY ATTRIBUTABLE TO EQUITY HOLDERS OF THE COMPANY:	13			
Share capital		1,399	5,441	4,037
Share premium		77,600	301,787	267,946
Capital reserve from share-based payment transactions		4,411	17,153	15,761
Warrants exercisable into shares (Series 9-12)		2,481	9,652	9,652
Treasury shares, at cost		(933)	(3,628)	(3,628)
Accumulated other comprehensive loss		(261)	(1,015)	(151)
Accumulated deficit		(78,207)	(304,150)	(280,391)
Total equity attributable to equity holders of the company		6,490	25,240	13,226
Non-controlling interests		375	1,460	2,299
Total shareholders' equity		6,865	26,700	15 525
Total liabilities and shareholders' equity		10,200	39,667	23,105

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

In thousands (except for share and per share data)

	Note	Year ended December 31,			
		2014	2014	2013	2012
		USD	NIS		
		Note 2.c.2			
Research and development expenses	15	4,165	16,200	15,390	13,160
General and administrative expenses	16	2,976	11,573	15,922	9,272
Operating loss		7,141	27,773	31,312	22,432
Financial expenses	17	316	1,228	892	59
Financial income	17	(1,157)	(4,500)	(1,401)	(573)
Loss before taxes on income		6,300	24,501	30,803	21,918
Taxes on income	19	6	23	9	11
Net loss		6,306	24,524	30,812	21,929
Other comprehensive loss (income):					
Adjustments arising from translating financial statements of foreign operations		241	939	206	(7)
Remeasurement loss (gain) from defined benefit plans		24	94	49	(42)
Total other comprehensive loss (income)		265	1,033	255	(49)
Total comprehensive loss		6,571	25,557	31,067	21,880
Net loss Attributable to:					
Equity holders of the Company		6,109	23,759	29,049	20,862
Non-controlling interests		197	765	1,763	1,067
		6,306	24,524	30,812	21,929
Total comprehensive loss attributable to:					
Equity holders of the Company		6,331	24,623	29,267	20,811
Non-controlling interests		240	934	1,800	1,069
		6,571	25,557	31,067	21,880
Net loss per share attributable to equity holders of the Company:					
Basic and diluted net loss per share	18	0.35	1.35	2.12	2.08

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

In thousands (except for share and per share data)

	Attributable to equity holders of the Company									
	Share capital	Share premium	Capital reserve from share-based payment transactions	Warrants exercisable into shares	Treasury shares	Accumulated other comprehensive income (loss)	Accumulated deficit	Total	Non-controlling interests	Total Equity (deficiency)
	NIS									
Balance as of January 1, 2012	2,606	229,299	14,670	-	(5,805)	16	(230,480)	10,306	2,221	12,527
Net loss	-	-	-	-	-		(20,862)	(20,862)	(1,067)	(21,929)
Adjustments arising from translating financial statements of foreign operations	-	-	-	-	-	9	-	9	(2)	7
Remeasurement gain (loss) from defined benefit plans	-	-	-	-	-	42	-	42	-	42
Total comprehensive loss	-	-	-	-	-	51	(20,862)	(20,811)	(1,069)	(21,880)
Exercise of unlisted share options	5	171	-	-	-	-	-	176	-	176
Exercise of warrants (Series 5)	1	75	-	-	-	-	-	76	-	76
Issuance of share capital and warrants (Series 9 net of issue expenses of NIS 491 thousand)	122	4,209	-	669	-		-	5,000	-	5,000
Share-based payments	-	-	609	-	-	-	-	609	847	1,456
Balance as of December 31, 2012	2,734	233,754	15,279	669	(5,805)	67	(251,342)	(4,644)	1,999	(2,645)

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

In thousands (except for share and per share data)

	Attributable to equity holders of the Company									
	Share capital	Share premium	Capital reserve from share-based payment transactions	Warrants exercisable into shares	Treasury shares	Accumulated other comprehensive income (loss)	Accumulated deficit	Total	Non-controlling interests	Total Equity
	NIS									
Balance as of January 1, 2013	2,734	233,754	15,279	669	(5,805)	67	(251,342)	(4,644)	1,999	(2,645)
Net loss	-	-	-	-	-	-	(29,049)	(29,049)	(1,763)	(30,812)
Adjustments arising from translating financial statements of foreign operations	-	-	-	-	-	(169)	-	(169)	(37)	(206)
Remeasurement gain (loss) from defined benefit plans	-	-	-	-	-	(49)	-	(49)	-	(49)
Total comprehensive loss	-	-	-	-	-	(218)	(29,049)	(29,267)	(1,800)	(31,067)
Exercise of unlisted share options	87	-	-	-	-	-	-	87	-	87
Exercise of warrants (Series 8, Series 10 and Series 11)	1	41	-	-	-	-	-	42	-	42
Issuance of share capital and warrants (Series 12) net of issue expenses of NIS 3,749 thousands	1,206	34,083	283	2,739	-	-	-	38,311	-	38,311
Reclassification of warrants (Series 10 and Series 11)	-	-	-	6,244	-	-	-	6,244	-	6,244
Sale of treasury shares	-	(277)	-	-	2,177	-	-	1,900	(61)	1,839
Share-based payments	9	345	199	-	-	-	-	553	2,161	2,714
Balance as of December 31, 2013	4,037	267,946	15,761	9,652	(3,628)	(151)	(280,391)	13,226	2,299	15,525

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY (DEFICIENCY)

In thousands (except for share and per share data)

	Attributable to equity holders of the Company									
	Share capital	Share premium	Capital reserve from share-based payment transactions	Warrants exercisable into shares	Treasury shares	Accumulated other comprehensive income (loss)	Accumulated deficit	Total	Non-controlling interests	Total Equity
	NIS									
Balance as of January 1, 2014	4,037	267,946	15,761	9,652	(3,628)	(151)	(280,391)	13,226	2,299	15,525
Net loss	-	-	-	-	-	-	(23,759)	(23,759)	(765)	(24,524)
Adjustments arising from translating financial statements of foreign operations	-	-	-	-	-	(770)	-	(770)	(169)	(939)
Remeasurement gain (loss) from defined benefit plans	-	-	-	-	-	(94)	-	(94)	-	(94)
Total comprehensive loss	-	-	-	-	-	(864)	(23,759)	(24,623)	(934)	(25,557)
Issuance of share capital and warrants, net of issue expenses of NIS 3,845	1,390	33,522	994	-	-	-	-	35,906	-	35,906
Share-based payments	14	319	398	-	-	-	-	731	95	826
Exercise of unlisted share options	*)	*)	-	-	-	-	-	-	-	-
Balance as of December 31, 2014	5,441	301,787	17,153	9,652	(3,628)	(1,015)	(304,150)	25,240	1,460	26,700

*) Represent an amount lower than NIS 1.

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

In thousands (except for share and per share data)

	Attributable to equity holders of the Company									
	Share capital	Share Premium	Capital reserve from share-based payment transactions	Warrants exercisable into shares	Treasury shares	Accumulated other comprehensive income (loss)	Accumulated deficit	Total	Non-controlling interests	Total Equity
	USD (Note 2.c.2)									
Balance as of January 1, 2014	$ 1,038	$ 68,898	$ 4,053	$ 2,481	$ (933)	$ (39)	$ (72,098)	$ 3,400	$ 590	$ 3,990
Net loss	-	-	-	-	-	-	(6,109)	(6,109)	(197)	(6,306)
Adjustments arising from translating financial statements of foreign operations	-	-	-	-	-	(198)	-	(198)	(43)	(241)
Remeasurement gain (loss) from defined benefit plans	-	-	-	-	-	(24)	-	(24)	-	(24)
Total comprehensive loss	-	-	-	-	-	(222)	(6,109)	(6,331)	(240)	(6,571)
Exercise of unlisted share options	*)	*)	-	-	-	-	-	-	-	-
Issuance of share capital and warrants, net of issue expenses of USD 989 thousands	357	8,620	256	-	-	-	-	9,233	-	9,233
Share-based payments	4	82	102	-	-	-	-	188	25	213
Balance as of December 31, 2014	$ 1,399	$ 77,600	$ 4,411	$ 2,481	$ (933)	$ (261)	$ (78,207)	$ 6,490	$ 375	$ 6,865

*) Represent an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CASH FLOWS
In thousands (except for share and per share data)

	Year ended December 31,			
	2014	2014	2013	2012
	USD	NIS		
	Note 2.c.2			
Cash flows from operating activities:				
Net loss	(6,306)	(24,524)	(30,812)	(21,929)
Adjustments to reconcile loss to net cash used:				
Depreciation of property, plant and equipment	12	47	58	86
Share-based payment	213	826	2,714	1,456
Issuance expenses related to warrants exercisable into shares	301	1,170	651	32
Gain from sale of property, plant and equipment	-	-	(6)	(42)
Increase (decrease) in severance pay, net	*)	1	12	(80)
Changes in fair value of warrants exercisable into shares	(794)	(3,089)	(1,309)	(429)
Exchange differences on balances of cash and cash equivalents	201	782	(559)	(217)
	(67)	(263)	1,561	806
Working capital adjustments:				
Decrease (increase) in accounts receivable, prepaid expenses and lease deposit	(304)	(1,181)	(555)	2,088
Increase (decrease) in trade payable	(275)	(1,069)	(766)	891
Increase (decrease) in other accounts payable	(385)	(1,495)	516	1,900
	(964)	(3,745)	(805)	4,879
Net cash used in operating activities	(7,337)	(28,532)	(30,056)	(16,244)

*) Represent an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CASH FLOWS

In thousands (except for share and per share data)

	Year ended December 31,			
	2014	2014	2013	2012
	USD	NIS		
	Note 2.c.2			
Cash flows from investing activities:				
Purchase of property, plant and equipment	(10)	(37)	(43)	(17)
Proceeds from sale of property, plant and equipment	-	-	7	92
Net cash provided by (used in) investing activities	(10)	(37)	(36)	75
Cash flows from financing activities:				
Issuance of share capital and warrants, net of issuance expenses	11,488	44,675	44,054	5,349
Exercise of unlisted share options	**)	*)	87	176
Exercise of share warrants (Series 5, 8, 10 and 11)	-	-	42	76
Sale of treasury shares	-	-	1,839	-
Net cash provided by financing activities	11,488	44,675	46,022	5,601
Exchange differences on balances of cash and cash equivalents	(201)	(782)	559	224
Increase (decrease) in cash and cash equivalents	3,940	15,324	16,489	(10,344)
Cash and cash equivalents at the beginning of the year	5,340	20,767	4,278	14,622
Cash and cash equivalents at the end of the year	9,280	36,091	20,767	4,278
Supplemental disclosure of cash flow information:				
Cash paid during the year for income taxes	2	9	-	11
Cash received during the year for interest	11	42	31	50

*) Represent an amount lower than NIS 1.
**) Represent an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1:- GENERAL

a. Company description:

Can-Fite Biopharma Ltd. was incorporated and started to operate in September 1994 as a private Israeli company. The Company is engaged in the development of drugs and medical diagnosis tools and is in the development stage of its products and has no sales yet (except exclusive license agreements, see Note 12). On October 6, 2005, the Company conducted an initial offering of securities to the public in Israel pursuant to a prospectus which it had published (TASE: CFBI).

On October 4, 2012, the Company announced the beginning of Level 1 OTC trading of its American Depository Shares ("ADSs") in the U.S. On September 12, 2013, the Company started to trade in level 2 ADSs in the OTC US. On November 19, 2013 the Company's level 2 ADSs began trading on the NYSE MKT under the symbol CANF.

b. During 2006, the Company founded a subsidiary in the UK under the name of Ultratrend Limited whose main purpose is to focus on coordinating the logistics for the multi-national PHASE IIb clinical studies. As of the reporting date, Ultratrend Limited has not commenced its operations.

c. The Company has a U.S. based subsidiary, OphthaliX Inc., owned 82% by the Company, which is developing the CF101 drug for treatment of ophthalmic indications. The license to develop this drug was transferred from the Company to OphthaliX Inc. in the context of the ophthalmic activity spinoff transaction, see Note 5 below. OphthaliX Inc. is traded over the counter in the U.S. (OTCQB: OPLI).

d. During the year ended December 31, 2014, the Company incurred losses of NIS 24,524 thousand and it has negative cash flows from operating activities in the amount of NIS 28,532 thousand as well as accumulated losses from previous years. The Company has not yet generated any material revenues from the sale of its own developed products and has financed its activities by raising capital and by collaborating with multinational companies in the industry. In March, 2014 and December, 2014, the Company raised a net total of NIS 15,772 thousand (approximately $4,545 thousand) and NIS 28,903 thousand (approximately $7,237 thousand) respectively, see Note 13d). Furthermore, the Company is continuing to finance its operating activities by raising capital and collaborating with multinational companies in the industry. The Company has other alternative plans for financing its ongoing activities, if necessary, such as improving the Company's flexibility in the patient recruitment rate of its clinical trials and/or the sale of assets.

In February 2013, as updated in March 2015, the Company issued a formal letter to OphthaliX, pursuant to which it agrees that OphthaliX will defer payments to Company under the services agreement from January 31, 2013 for the performance of the clinical trials of CF101 in ophthalmic indications until the completion of a fundraising by OphthaliX that will allow such payment. In addition, in March 2015 the Company issued a financial support letter, pursuant to which it is committed to cover any shortfall in the costs and expenses of operations of OphthaliX which are in excess of the OphthaliX's available cash to finance its operations, including cash generated from any future sale of the Can-Fite shares. Both letters are for a period of at least 14 months from March 2015 and any related balance bears interest at a rate of 3% per annum.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1:- GENERAL (Cont.)

The Company's management and board of directors are of the opinion that these financial resources will be used for operating activities for at least twelve months. There are no assurances that the Company will have an adequate level of financing needed for its long-term research and development activities. If the Company will not have sufficient liquidity resources, the Company may not be able to continue the development of all of its products or may be required to delay part of the development programs.

e. Definitions:

In these consolidated financial statements:

The Company	-	Can-Fite Biopharma Ltd.
The Group	-	The Company and its subsidiaries (as defined below).
Subsidiaries	-	Companies that are controlled by the Company (as defined in IAS 27 (2008)) and whose accounts are consolidated with those of the Company.
OphthaliX	-	OphthaliX Inc.
Eye-Fite	-	Eye-Fite Ltd. (OphthaliX Inc.'s wholly owned subsidiary).
Related parties	-	As defined in IAS 24.
NIS	-	New Israeli Shekel
USD	-	U.S. dollar.
€	-	European Union Euro
CDN$	-	Canadian dollar

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES

The following accounting policies have been applied consistently in the financial statements for all periods presented, unless otherwise stated.

a. Basis of presentation of the financial statements

These financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board. The Company's financial statements have been prepared on a cost basis, except for financial assets and liabilities (including warrants) which are presented at fair value through statement of comprehensive loss.

The preparation of the financial statements requires management to make critical accounting estimates as well as exercise judgment in the process of adopting significant accounting policies. The matters which required the exercise of significant judgment and the use of estimates, which have a material effect on amounts recognized in the financial statements, are specified in Note 3.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

b. Consolidated financial statements

The consolidated financial statements comprise the financial statements of companies that are controlled by the Company (i.e., subsidiaries). Control exists when the Company has the power, directly or indirectly, to govern the financial and operating policies of an entity. The effect of potential voting rights that are exercisable at the end of the reporting period is considered when assessing whether an entity has control. The consolidation of the financial statements commences on the date on which control is obtained and ends when such control ceases.

The financial statements of the Company and of the subsidiaries are prepared as of the same dates and periods. The consolidated financial statements are prepared using uniform accounting policies by all companies in the Group. Significant intragroup balances and transactions and gains or losses resulting from intragroup transactions are eliminated in full in the consolidated financial statements.

Non-controlling interests of subsidiaries represent the non-controlling shareholders' share of the total comprehensive loss of the subsidiaries and their share of the net assets. The non-controlling interests are presented in equity separately from the equity attributable to the equity holders of the Company. Losses are attributed to non-controlling interests even if they result in a negative balance of non-controlling interests in the consolidated statement of financial position.

c. Functional currency, presentation currency and foreign currency:

1. Functional currency and presentation currency:

The functional currency of the Company and presentation currency of the financial statements is the NIS.

When a subsidiary’s functional currency differs from the Company's functional currency, the subsidiary financial statements are translated into the Company's functional currency so that they can be included in the consolidated financial statements.

Assets and liabilities are translated at the closing rate at the end of each reporting period.

Comprehensive loss items are translated at average exchange rates for all the relevant periods. All resulting translation differences are recognized as a separate component of other comprehensive loss in equity under “adjustments arising from translating financial statements”.

2. Convenience translation:

For the convenience of the reader, the reported NIS amounts as of December 31, 2014 have been translated into U.S. dollars, at the representative rate of exchange on December 31, 2014 (U.S. $1 = NIS 3.889). The U.S. dollar amounts presented in these financial statements should not be construed as representing amounts that are receivable or payable in dollars or convertible into U.S. dollars, unless otherwise indicated. The U.S. dollar amounts were rounded to whole numbers for convenience.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

3. Transactions, assets and liabilities in foreign currency:

Transactions denominated in foreign currency are recorded upon initial recognition at the exchange rate at the date of the transaction. After initial recognition, monetary assets and liabilities denominated in foreign currency are translated at the end of each reporting period into the functional currency at the exchange rate at that date. Exchange rate differences are recognized in statement of comprehensive loss. Non-monetary assets and liabilities measured at cost in foreign currency are translated at the exchange rate at the date of the transaction. Non-monetary assets and liabilities denominated in foreign currency and measured at fair value are translated into the functional currency using the exchange rate prevailing at the date when the fair value was determined.

4. Index-linked monetary items:

Monetary assets and liabilities linked to the changes in the Israeli Consumer Price Index ("Israeli CPI") are adjusted at the relevant index at the end of each reporting period according to the terms of the agreement. Linkage differences arising from the adjustment, as above, are recognized in statement of comprehensive loss.

d. Cash equivalents

Cash equivalents are considered as highly liquid investments, including unrestricted short-term bank deposits with an original maturity of three months or less from the investment date.

e. Account receivables and prepaid expenses

Prepaid expenses are composed mainly from active pharmaceutical ingredients and clinical trials drug-kits which expense based on a percentage of completion method of the related clinical trials.

f. Property, plant and equipment

Property, plant and equipment are measured at cost, including directly attributable costs, less accumulated depreciation, accumulated impairment losses and excluding day-to-day servicing expenses.

Depreciation is calculated on a straight-line basis over the useful life of the assets at annual rates as follows:

	%	Mainly %
Laboratory equipment and Leasehold improvements	10	
Computers, office furniture and equipment	6 - 33	33

The useful life, depreciation method and residual value of an asset are reviewed at least each year-end and any changes are accounted for prospectively as a change in accounting estimates**.** Depreciation of an asset ceases at the earlier of the date that the asset is classified as held for sale and the date that the asset is derecognized. An asset is derecognized on disposal or when no further economic benefits are expected from its use. The gain or loss arising from the derecognition of the asset (determined as the difference between the net disposal proceeds and the carrying amount in the financial statements) is included in the statement of comprehensive loss when the asset is derecognized.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

g. Research and development expenditures

Research expenditures are recognized in the statement of comprehensive loss when incurred.

h. Impairment of non-financial assets

The Group evaluates the need to record an impairment of the carrying amount of property, plant and equipment whenever events or changes in circumstances indicate that the carrying amount is not recoverable. If the carrying amount of property, plant and equipment exceeds their recoverable amount, the property, plant and equipment are reduced to their recoverable amount. The recoverable amount is the higher of fair value less costs of sale and value in use. In measuring value in use, the expected future cash flows are discounted using a pre-tax discount rate that reflects the risks specific to the asset. As of December 31, 2014 and 2013, no impairment losses have been identified.

i. Financial instruments

1. Financial liabilities

Financial liabilities within the scope of IAS 39 are classified as either financial liabilities at fair value through statement of comprehensive loss.

The Group determines the classification of the liability on the date of initial recognition. All liabilities are initially recognized at fair value. After initial recognition, the accounting treatment of financial liabilities is based on their classification as follows:

Financial liabilities at fair value through statement of comprehensive loss

Financial liabilities at fair value through profit or loss include financial liabilities designated upon initial recognition as at fair value through statement of comprehensive loss.

A liability may be designated upon initial recognition at fair value through profit or loss, subject to the provisions of IAS 39.

2. Fair value

The fair value of financial instruments that are traded in an active market is determined by reference to market prices at the end of the reporting period. For financial instruments where there is no active market, fair value is determined using valuation techniques. Such techniques include using recent arm's length market transactions, reference to the current market value of another instrument which is substantially the same, discounted cash flow and other valuation models. A detailed analysis of the fair value measurement of financial instruments is provided in Note 10 below.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

3. Issue of a unit of securities

The issue of a unit of securities involves the allocation of the proceeds received (before issue expenses) to the components of the securities issued in the unit based on the following order: financial derivatives and other financial instruments measured at fair value in each period. Then fair value is determined for financial liabilities and compound instruments that are presented at amortized cost. The consideration allocated to the equity instruments is determined as the residual value. The issuance costs are allocated to each component based on the amounts allocated to each component in the unit.

4. Derecognition of financial instruments

Financial liabilities:

A financial liability is derecognized when it is extinguished, that is when the obligation is discharged, realized, cancelled or expires. A financial liability is extinguished when the debtor (i.e., the Group) discharges the liability by paying in cash, other financial assets, goods or services or shares, or is legally released from the liability.

When an existing financial liability is exchanged with another liability from the same lender on substantially different terms, or the terms of an existing liability are substantially modified, such an exchange or modification is accounted for as an extinguishment of the original liability and the recognition of a new liability. The difference between the carrying amount of the above liabilities is recognized in statement of comprehensive loss. If the exchange or modification is not substantial, it is accounted for as a change in the terms of the original liability and no gain or loss is recognized on the exchange.

j. Treasury shares

Company shares held by OphthaliX are recognized at cost and deducted from equity. Any gain or loss arising from a purchase, sale, issuance or cancellation of treasury shares is recognized directly in equity.

k. Provisions

A provision in accordance with IAS 37 is recognized when the Group has a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation. If the Group expects part or all of the expense to be reimbursed to the Company, such as in an insurance contract, the reimbursement is recognized as a separate asset only when it is virtually certain that it will be received by the Company. The expense is recognized in the income statement net of the reimbursed amount.

No provisions pursuant to IAS 37 have been identified.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

l. Employee benefit liabilities

The Group has several employee benefit plans:

1. Short-term employee benefits:

Short-term employee benefits include salaries and social security contributions are recognized as expenses as the services are rendered. A liability in respect of a cash bonus is recognized when the Group has a legal or constructive obligation to make such payment as a result of past service rendered by an employee and a reliable estimate of the amount can be made.

2. Post-employment benefits:

The post-employment benefit plans are normally financed by contributions to insurance companies and classified as defined benefit plans.

The Company operates a defined benefit plan in respect of severance pay pursuant to the Severance Pay Law. According to the Severance Pay Law, employees are entitled to severance pay upon dismissal or retirement. The liability for termination of employment is measured using the projected unit credit method. The actuarial assumptions include rates of employee turnover and future salary increases based on the estimated timing of payment. The amounts are presented based on discounted expected future cash flows using a discount rate determined by reference to yields on government bonds with a term that matches the estimated term of the benefit obligation.

In respect of its severance pay obligation to certain of its employees, the Company makes current deposits in pension funds and insurance companies (the "Plan Assets"). Plan Assets comprise assets held by a long-term employee benefit fund or qualifying insurance policies. Plan Assets are not available to the Company's own creditors and cannot be returned directly to the Company.

The liability for employee benefits shown in the statement of financial position reflects the present value of the defined benefit obligation less the fair value of the plan assets, less past service costs.

Actuarial gains and losses are recognized in other comprehensive loss.

As for effects of the change in the type of bonds used in determining the discount rate**,** see Note 1 q below.

m. Share-based payment transactions

The Company's employees and other service providers are entitled to remuneration in the form of equity-settled share-based payment transactions and certain employee and other service providers are entitled to remuneration in the form of share-based payment transactions that are measured based on the increase in the Company's share price.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

The cost of equity-settled transactions with employees is measured at the fair value of the equity instruments granted at grant date. The fair value is determined using the Binomial option pricing model.

As for other service providers, the cost of the transactions is measured at the fair value of the goods or services received as consideration for equity instruments. In cases where the fair value of the goods or services received as consideration of equity instruments cannot be measured, they are measured by reference to the fair value of the equity instruments granted using Black-Scholes-Merton option pricing model.

The cost of equity-settled transactions is recognized in statement of comprehensive loss, together with a corresponding increase in equity, during the period which the performance and/or service conditions are to be satisfied, ending on the date on which the relevant employees become fully entitled to the award (the "Vesting Period"). The cumulative expense recognized for equity-settled transactions at the end of each reporting period until the vesting date reflects the extent to which the Vesting Period has expired and the Group's best estimate of the number of equity instruments that will ultimately vest. The expense or income recognized in statement of comprehensive loss represents the change between the cumulative expense recognized at the end of the reporting period and the cumulative expense recognized at the end of the previous reporting period.

If the Company modifies the conditions on which equity-instruments were granted, an additional expense is recognized for any modification that increases the total fair value of the share-based payment arrangement or is otherwise beneficial to the employee/other service provider at the modification date.

n. Taxes on income

As it is not likely that taxable income will be generated in the foreseeable future, deferred tax assets due to accumulated losses is not recognized in the Group's financial statements.

o. Loss per share

Losses per share are calculated by dividing the net loss attributable to equity holders of the Company by the weighted number of ordinary shares outstanding during the period. Potential ordinary shares (warrants and unlisted options) are only included in the computation of diluted loss per share when their conversion increases loss per share from continuing operations. Potential ordinary shares that are converted during the period are included in diluted loss per share only until the conversion date and from that date in basic loss per share. The Company's share of loss of subsidiary is included based on the loss per share of OphthaliX multiplied by the number of shares held by the Company.

p. Reclassification:

Certain amounts in prior years have been reclassified to conform to the current year's presentation.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

q. Changes in estimates:

In November 2014, the staff of the Israel Securities Authority issued Accounting Position Paper No. 21-1 regarding the existence in Israel of a deep market in high quality corporate bonds (the "Position Paper") for the purpose of determining, in accordance with IAS 19, the discount rate to be used for defined benefit obligations and other long-term benefits in the Israeli currency. According to the Position Paper, the transition from the use of yields based on Government bonds (2.34%) to market yields based on high quality corporate bonds linked to the Consumer Price Index (3.11%) should be accounted for prospectively as a change in accounting estimate.

The effects of the change in the above mentioned discount rate are immaterial.

NOTE 3:- SIGNIFICANT ACCOUNTING JUDGMENTS, ESTIMATES AND ASSUPMTIONS USED IN THE PREPARATION OF THE FINANCIAL STATEMENTS

In the process of applying the significant accounting policies, the Group has made the following judgments which have the most significant effect on the amounts recognized in the financial statements:

a. Judgments

Determining the fair value of share-based payment transactions

The fair value of share-based payment transactions is determined using an acceptable option-pricing model. The model includes data as to the share price and exercise price, and assumptions regarding expected volatility, expected life, expected dividend and risk-free interest rate.

b. Estimates and assumptions

The preparation of the financial statements requires management to make estimates and assumptions that have an effect on the application of the accounting policies and on the reported amounts of assets, liabilities and expenses.

Changes in accounting estimates are reported in the period of the changes in estimates.

The key assumptions made in the financial statements concerning uncertainties at the end of the reporting period and the critical estimates computed by the Group that may result in a material adjustment to the carrying amounts of assets and liabilities within the next financial year are discussed below.

Post-employment benefits

The liability in respect of post-employment defined benefit plans is determined using actuarial valuations. The actuarial valuation involves making assumptions about, among others, discount rates, expected rates of return on assets, future salary increases and mortality rates. The carrying amount of the liability may be significantly affected by changes in such estimates.

NOTE 4:- DISCLOSURE OF NEW STANDARDS IN THE PERIOD PRIOR TO THEIR ADOPTION

IFRS 9-Financial Instruments:

In July 2014, the IASB issued the final version of IFRS 9 Financial Instruments which reflects all phases of the financial instruments project and replaces IAS 39 Financial Instruments: Recognition and Measurement and all previous versions of IFRS 9. The standard introduces new requirements for classification and measurement, impairment, and hedge accounting. IFRS 9 is effective for annual periods beginning on or after 1 January 2018, with early application permitted.

The adoption of IFRS 9 will have no material effect on the Company's financial assets on the financial statements.

NOTE 5:- OPHTHALIX SPIN OFF

a. Purchase agreement

On November 21, 2011, the Company consummated the acquisition of 82% of the issued and outstanding share capital of OphthaliX Inc.

The spin-off was consummated pursuant to an agreement dated June 5, 2011 (the "Spin-Off Agreement") to spin-off the Company's activity in the ophthalmology field to OphthaliX and, based on its conditions, the following agreements were signed:

1. The Spin-Off Agreement

According to the Spin-Off Agreement, the Company transferred to OphthaliX 100% of the issued and outstanding capital of Eye-Fite, the Company's former wholly-owned subsidiary, such that Eye-Fite became the wholly-owned subsidiary of OphthaliX in exchange for 8,000,000 shares of OphthaliX common stock, representing 86.7% of OphthaliX's issued and outstanding capital. In addition, the Company received 466,139 shares of OphthaliX common stock in exchange for 714,922 ordinary shares of the Company pursuant to the terms of a material private placement that the Company effected on November 21, 2011 at a price of $5.148 per share, which reflected a value for OphthaliX of approximately $50 million before the transfer of the Company's ordinary shares, described above, and before the material private placement fundraising for OphthaliX (the key elements of which are described below). The Company purchased 97,113 shares of OphthaliX common stock in the same private placement at the same price per share, or a purchase price of $5.148 per share.

Upon the closing of the transactions contemplated by the spin-off agreement, the Company appointed all of the members of OphthaliX's board of directors (three members of which are also members of the Company's board of directors). According to the spin-off agreement, OphthaliX will, among other things, continue the development processes, clinical trials and registration of the ophthalmic indications for CF101. The Company will provide certain services to OphthaliX under the services agreement detailed below.

NOTE 5:- OPHTHALIX SPIN OFF (Cont.)

The transaction was accounted for in the consolidated financial statements of Can-Fite as a continuation of the financial statements of Eye-Fite, together with a deemed issuance of shares to the pre-acquisition shareholders of Ophthalix. The deemed issuance of shares was in consideration for the listing of Eye-Fite in the U.S, and therefore it is in effect a share-based payment transaction.

The share-based payment transaction was accounted for in accordance with IFRS 2 "Share based payment". Consequently, the financial statements include a charge of NIS 11,060 thousand that represents the value of OphthaliX shares before the transaction. Additional issuance expenses in an amount of NIS 436 thousand were recorded in the consolidated statements of comprehensive loss report.

2. Eye-Fite License agreement

A license agreement was entered into between the Company and Eye-Fite (the "Eye-Fite License Agreement") according to which the Company granted Eye-Fite a non-transferrable exclusive license, as set forth in the Eye-Fite License Agreement, for the use of the Company's know-how solely in the field of ophthalmic diseases for research, development, commercialization and marketing throughout the world. Eye-Fite is permitted to sublicense subject to the Eye-Fite License Agreement. As consideration for the grant of the license according to the Eye-Fite License Agreement, the Company received 1,000 ordinary shares of Eye-Fite, par value NIS 0.01 per share, representing 100% of the issued and outstanding share capital of Eye-Fite.

According to the Eye-Fite License Agreement with the U.S. National Institute of Health, the Centers for Disease Control and Prevention ("NIH"), Eye-Fite is obligated to make royalty payments to NIH.

All inventions resulting from the indication that is licensed thereunder shall belong to the Company whether it was invented solely by it, solely by Eye-Fite or by both in cooperation. However, the Company granted Eye-Fite an exclusive license to use these inventions in the field of ophthalmic diseases around the world at no consideration. The license will remain in effect until the expiration of the last patent licensed thereunder unless it is terminated sooner by a mutual agreement in writing or by one of the parties according to the clauses of the Eye-Fite License Agreement.

3. Services agreement

In addition to the Eye-Fite License Agreement, the Company, OphthaliX and Eye-Fite entered into a services agreement (the "Services Agreement") pursuant to which the Company provides management services with respect to all pre-clinical and clinical research studies, production and supply of the compounds related to the Eye-Fite License Agreement and payment for consultants that are listed in the agreement for their involvement in the clinical trials and in all the activities leading up to, and including, the commercialization of CF101 for ophthalmic indications.

NOTE 5:- OPHTHALIX SPIN OFF (Cont.)

As consideration for the rendering of services, as above, the Company will be paid only for its costs and expenses incurred in rendering the services plus 15%, as well as reimbursed for the expenses actually charged for the maintenance of patents underlying the license to Eye-Fite.

In February 2013, the Company sent a formal letter to OphthaliX, which has been updated periodically (most recently in March 2015), agreeing to defer payments owed to the Company under the Services Agreement beginning on January 31, 2013 for the performance of the clinical trials of CF101 in ophthalmic indications until the completion of fundraising by OphthaliX sufficient to cover such deferred payments. The letter remains in effect for a period of at least 14 months from March 2015 and any related balance bears interest at a rate of 3% per annum.

Further, the Company will be entitled to an additional payment of 2.5% of any revenues received by the Group for the rights to use the transferred know-how (the "Additional Payment").

The Company is entitled during a 5-year period from the date of the approval of the Services Agreement, to convert its right to the Additional Payment into 480,023 shares of OphthaliX (representing about 5% of OphthaliX shares on a fully diluted basis as of the date of closing the spin-off agreement) in consideration for the exercise price set forth in the services agreement. The Services Agreement shall remain in force for an unlimited period of time.

4. Pre-ruling from the Income Tax

The Company received a pre-ruling decision from the Israeli Income Tax Authority which confirms (1) that the grant of the license to Eye-Fite is not liable for tax pursuant to the provisions of section 104a to the Income Tax Ordinance (New Version), 1961 ("the Ordinance"); (2) that OphthaliX is considered the receiving company pursuant to section 103c(7)(b) to the Ordinance; (3) that the sale of Eye-Fite shares to OphthaliX as consideration for OphthaliX shares does not create liability for tax pursuant to the provisions of section 103t to the Ordinance ("Change in Structure"); and (4) the date for the Change in Structure was determined. According to the tax pre-ruling, the date of Change in Structure shall also be the date of exchange of shares with respect to the spin-off and notification to the tax assessor. The Company and Eye-Fite presented to the tax assessor and the merger and spin-off department of the tax assessor the forms required by the Ordinance and the regulations thereunder. The tax pre-ruling further provides that the grant of a license to Eye-Fite as consideration for the issuance of Eye-Fite shares to the Company does not create liability for tax pursuant to the provisions of section 104a to the Ordinance.

NOTE 6:- ACCOUNTS RECEIVABLE AND PREPAID EXPENSES

	December 31,	
	2014	2013
	NIS in thousands	
Government authorities	272	201
Prepaid expenses and others	3,145	1,960
	3,417	2,161

NOTE 7:- PROPERTY, PLANT AND EQUIPMENT, NET

Balance as of December 31, 2014:

	Laboratory equipment	Computers, office furniture and equipment	Leasehold improvements	Total
	NIS in thousands			
Cost:				
Balance at January 1, 2014	880	1,052	646	2,578
Purchases during the year	3	34	-	37
Balance at December 31, 2014	883	1,086	646	2,615
Accumulated depreciation:				
Balance at January 1, 2014	844	959	632	2,435
Depreciation during the year	7	38	2	47
Balance at December 31, 2014	851	997	634	2,482
Depreciated cost at December 31, 2014	32	89	12	133

Balance as of December 31, 2013:

	Laboratory equipment	Computers, office furniture and equipment	Leasehold improvements	Total
	NIS in thousands			
Cost:				
Balance at January 1, 2013	930	1,026	646	2,602
Purchases during the year	17	26	-	43
Disposals during the year	(67)	-	-	(67)
Balance at December 31, 2013	880	1,052	646	2,578
Accumulated depreciation:				
Balance at January 1, 2013	902	909	632	2,443
Depreciation during the year	8	50	-	58
Disposals during the year	(66)	-	-	(66)
Balance at December 31, 2013	844	959	632	2,435
Depreciated cost at December 31, 2013	36	93	14	143

NOTE 8:- TRADE PAYABLES

	December 31,	
	2014	2013
	NIS in thousands	
Trade Payables	995	1,782
Checks payable	29	274
	1,024	2,056

NOTE 9:- OTHER ACCOUNTS PAYABLE

	December 31,	
	2014	2013
	NIS in thousands	
Employees and payroll accruals	969	954
Accrued expenses	3,781	4,322
	4,750	5,276

NOTE 10:- FINANCIAL INSTRUMENTS

a. Classification of financial assets and liabilities

The financial assets and financial liabilities in the statement of financial position are classified by groups of financial instruments pursuant to IAS 39:

	December 31,	
	2014	2013
	NIS in thousands	
Financial assets:		
Account receivables	272	201
Financial liabilities:		
Trade payable	1,024	2,056
Other account payable	4,750	5,276
Warrants exercisable into shares	6,969	119
	12,743	7,451

b. Financial risks factors

The Group's activities expose it to foreign exchange risk. The Group's comprehensive risk management plan focuses on activities that reduce to a minimum any possible adverse effects on the Group's financial performance.

The Company's management identifies and manages financial risks.

NOTE 10:- FINANCIAL INSTRUMENTS (Cont.)

c. Foreign exchange risk

The Group is exposed to foreign exchange risk resulting from the exposure to different currencies, mainly the U.S. dollar. Foreign exchange risk arises on recognized assets and liabilities that are denominated in a foreign currency other than the functional currency.
The Group acts to reduce the foreign exchange risk by managing an adequate part of the available liquid sources in or linked to the dollar.

d. Fair value

The carrying amount of cash and cash equivalents, accounts receivable, trade payables and other accounts payable approximate their fair value.

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. To increase the comparability of fair value measures, the following hierarchy prioritizes the inputs to valuation methodologies used to measure fair value:

Level 1 - Valuations based on unadjusted quoted prices for identical assets and liabilities in active markets.

Level 2 - Valuations based on observable inputs other than quoted prices included in Level 1, such as quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets and liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data.

Level 3 - Valuations based on unobservable inputs reflecting assumptions, consistent with reasonably available assumptions made by other market participants. These valuations require significant judgment.

The company's warrants exercisable into shares are classified as level 3 in the fair value hierarchy.

e. Linkage terms of financial instruments

	December 31, 2014			
	In or linked to dollar	In or linked to Euro	Unlinked	Total
	NIS in thousands			
Assets:				
Cash and cash equivalents	31,412	1,613	3,066	36,091
Accounts receivable	-	-	272	272
	31,412	1,613	3,338	36,363
Liabilities:				
Trade payables	767	24	233	1,024
Other accounts payable	2,509	426	1,815	4,750
Warrants exercisable into shares	6,969	-	-	6,969
	10,245	450	2,048	12,743
Financial instruments, net	21,167	1,163	1,290	23,620

NOTE 10:- FINANCIAL INSTRUMENTS (Cont.)

	December 31, 2013				
	In or linked to dollar	In or linked to Euro	Linked to Israeli CPI	Unlinked	Total
	NIS in thousands				
Assets:					
Cash and cash equivalents	9,609	1,052	-	10,106	20,767
Accounts receivable	-	-	-	201	201
	9,609	1,052	-	10,307	20,968
Liabilities:					
Trade payables	1,568	43	-	445	2,056
Other accounts payable	2,339	1,425	-	1,512	5,276
Warrants exercisable into shares (Series 7)	-	-	119	-	119
	3,907	1,468	119	1,957	7,451
Financial instruments, net	5,702	(416)	(119)	8,350	13,517

e. Sensitivity tests relating to changes in market factors

	December 31,	
	2014	2013
	NIS in thousands	
Sensitivity test to changes in the U.S. dollar exchange rate:		
Gain (loss) from the change on financial instruments:		
Increase of 10% in exchange rate	2,117	570
Decrease of 10% in exchange rate	(2,117)	(570)
Sensitivity test to changes in the market price of listed securities:		
Gain (loss) from the change:		
Increase of 10% in market price	(1,213)	(12)
Decrease of 10% in market price	1,155	12

* According to binomial model 10% increase in the market price of listed securities will increase the price of warrants exercisable into shares by approximately 17% and 10% decrease in the market price of listed securities will decrease the price of warrants exercisable into shares by approximately 17%.

Sensitivity tests and the main work assumptions:

The selected changes in the relevant risk variables were determined based on management's estimate as to reasonable possible changes in these risk variables.

NOTE 10:- FINANCIAL INSTRUMENTS (Cont.)

The Group has performed sensitivity tests of principal market risk factors that are liable to affect its reported operating results or financial position. The sensitivity tests present the statement of comprehensive loss in respect of each financial instrument for the relevant risk variable chosen for that instrument as of each reporting date. The test of risk factors was determined based on the materiality of the exposure of the operating results or financial condition of each risk with reference to the functional currency and assuming that all the other variables are constant.

Based on the Group's policy, the Group generally mitigates the currency risk arising from recognized assets and recognized liabilities denominated in foreign currency other than the functional currency by maintaining part of the available liquid sources in deposits in foreign currency. Accordingly, the main currency exposures presented in the sensitivity tables are for those deposits.

NOTE 11:- EMPLOYEE BENEFIT LIABILITIES, NET

Employee benefits consist of short-term benefits and post-employment benefits.

Post-employment benefits

According to the labor laws and Severance Pay Law in Israel, the Company is required to pay compensation to an employee upon dismissal or retirement or to make current contributions in defined contribution plans pursuant to section 14 to the Severance Pay Law, as specified below. The Company's liability is accounted for as a post-employment benefit. The computation of the Company's employee benefit liability is made in accordance with a valid employment contract based on the employee's salary and employment term which establish the entitlement to receive the compensation.

In 2009, management accepted a decision according to which although section 14 applies, as above, the Company would pay all compensation upon dismissal of employees pursuant to the conditions of the Severance Pay Law.

In accordance with the above mentioned, since 2009, the Group does not contribute to defined contribution plans, but only to defined benefit plans.

The post-employment employee benefits are financed by contributions classified as a defined benefit plan as follows:

A defined benefit plan:

The Company accounts for the part of the compensation payments as a defined benefit plan for which an employee benefits liability is recognized and for which the Company deposits amounts in qualifying insurance policies.

NOTE 11:- EMPLOYEE BENEFIT LIABILITIES, NET (Cont.)

a. Expenses recognized in statement of comprehensive loss:

	Year ended December 31,		
	2014	2013	2012
	NIS in thousands		
Current service cost	134	146	149
Interest cost on benefit obligation	39	32	36
Expected return on plan assets	(37)	(33)	(29)
Total employee benefit expenses	136	145	156
Actual return on plan assets	23	77	98

b. The plan liabilities, net:

	December 31,	
	2014	2013
	NIS in thousands	
Defined benefit obligation	(1,238)	(1,120)
Fair value of plan assets	1,014	991
Total liabilities, net	(224)	(129)

c. Changes in the present value of defined benefit obligation:

	2014	2013
	NIS in thousands	
Balance at beginning of year	(1,120)	(849)
Recognized in statement of comprehensive loss:		
Interest cost	(39)	(32)
Current service cost	(134)	(146)
Recognized in other comprehensive loss:		
Net actuarial loss	(80)	(93)
Other:		
Benefits paid	135	-
Balance at end of year	(1,238)	(1,120)

d. Plan assets:

1) Plan assets comprise assets held by a long-term employee benefit fund and qualifying insurance policies.

NOTE 11:- EMPLOYEE BENEFIT LIABILITIES, NET (Cont.)

2) The movement in the fair value of the plan assets:

	2014	2013
	NIS in thousands	
Balance at beginning of year	991	781
Recognized in statement of comprehensive loss:		
Expected return	37	33
Recognized in other comprehensive loss:		
Net actuarial loss	(14)	44
Other:		
Contributions by employer	135	133
Withdrawals from the plan	(135)	-
Balance at end of year	1,014	991

e. The principal assumptions underlying the defined benefit plan:

	December 31,	
	2014	2013
	%	
Discount rate of the plan liability	3.11	3.73
Expected rate of return on plan assets	3.52	4.20
Future salary increases	3.50	3.50

f. Sensitivity tests to significant changes of:

		Increase (decrease) of the plan liabilities, net	
		December 31, 2014	
	Rate of change	Increase in Rate of change	Decrease in Rate of change
	%	NIS in thousands	
Salary	1	101	(61)
Interest	0.5	(33)	44
Israeli CPI	0.5	(4)	5
Employees turnover	20	(1)	2

NOTE 12:- CONTINGENT LIABILITIES AND COMMITMENTS

a. Liabilities to pay royalties:

1. According to the license agreement signed on January 29, 2003 with the U.S. National Institute of Health ("NIH") (through the US Public Health Service, "PHS") (the "PHS Agreement"), the Company is committed to pay royalties as follows:

   a) A minimum annual payment of $50 thousand, which is non-refundable.

   b) 4%-5.5% of the Company's total net revenues from sales of licensed products or from conducting tests, as defined in the PHS Agreement, on a consolidated basis, out of which 1.75%-2.75% may be offset against royalties that the Company is required to pay another third party. As of December 31, 2014, no accrual or payment has been made hereunder.

   c) Royalties in a total of up to $700 thousand per indication, subject to meeting certain drug development milestones as defined in the PHS Agreement as follows: (i) $25 thousand upon first Phase I initiation per indication; (ii) $75 thousand upon first Phase II initiation per indication; (iii) $100 thousand upon first Phase III initiation per indication; and (iv) $500 thousand upon approval by the FDA or any other regulatory authority. As of December 31, 2014, the Company accrued additional amount of NIS 1,653 thousand ($ 425 thousand).

   d) Additional payments totaling 20% of total payments received from any sub-licensee, out of which 2% may be offset against royalties that the Company is required to pay another third party. As of December 31, 2014, no accrual or payment has been made hereunder.

   The agreement will remain in effect until the expiration of the last patent, unless it is terminated sooner by one of the parties, according to the PHS Agreement.

   On February 4, 2013, a second revised agreement was signed for updating the milestone dates. These revised agreements have no effect on the original license terms.

2. According to the patent license agreement signed on November 2, 2009 with the Leiden University in the Netherlands, which is affiliated with the NIH, the Company is committed to pay royalties as follows:

   a) A one-time concession commission of € 25 thousand;
   b) Annual royalties of € 10 thousand until the clinical trials commence;
   c) 2%-3% of net sales (as defined in the agreement) received by the Company;
   d) Royalties in a total amount of up to €850 thousand based on certain progress milestones in the license stages of the products, which are the subject of the patent under the agreement, as follows: (i) €50 thousand upon initiation of Phase I studies; (ii) €100 thousand upon initiation of Phase II studies; (iii) €200 thousand upon initiation of Phase III studies; and (iv) €500 thousand upon marketing approval by any regulatory authority.
   e) If the agreement is sublicensed to another company, the Company will provide the Leiden University royalties at a rate of 10%. A merger, consolidation or any other change in ownership will not be viewed as an assignment of the agreement as discussed in this paragraph.

   As of December 31, 2014, no accrual is recorded with respect to Leiden University.

NOTE 12:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

b. Commitments and license agreements:

1. On September 22, 2006, the Company signed an exclusive license agreement regarding inflammatory indicators, including rheumatoid arthritis indicators (excluding eye disease indicators) with a public Japanese company, Seikagaku Corporation (the "Japanese Corporation"), for the use, development and marketing of the Company's CF101 drug in Japan only.

According to the agreement, the Company is entitled to receive the following amounts:

a) A non-refundable amount of $ 3 million (gross) (NIS 12,909 thousand) paid immediately upon signing the agreement. This amount was included in the Company's revenues in its financial statements for 2006.

b) An amount of $ 500 thousand (gross) on January 1 of each year starting from January 1, 2007, until the earlier of the date of filing an application for a new drug with the Japanese regulatory authorities and the beginning of the fifth year from the date of signing (until January 1, 2011).

c) An amount equal to $12 million (gross) based on the Japanese Corporation's progress milestones in the development of the CF101 for treating rheumatoid arthritis in Japan as follows: (i) $1 million following the commencement of a Phase I clinical trial of the CF101 drug by the Japanese Corporation (such amount was received and included in the Company's revenues in the year ended December 31, 2008); (ii) $5 million upon marketing authorization in Japan for the first indication; (iii) $1.5 million upon commencement of a Phase II clinical trial of the CF101 drug by the Japanese Corporation for the first indication in Japan; (vi) $2.5 million upon submission of a new drug application to the appropriate regulatory authority in Japan for the first indication; and (v) $2 million if the Japanese Corporation does not employ Bridging Strategy (as defined in the agreement) upon commencement of a Phase III clinical trial by the Japanese corporation for the first indication.

d) An aggregate amount of $ 2 million (gross) received in 2006 and 2007 ($ 1 million each year) based on milestones underlying the Company's Phase IIb clinical trial in rheumatoid arthritis indicators. These amounts were included in the Company's financial statements for said years under participation in research and development expenses, based on the milestones met by the Company according to the agreement.

e) If the Japanese Corporation decides to develop CF101 for the treatment of indications other than rheumatoid arthritis, the Company will be entitled to at least an additional $1 million (gross) based on milestones met in the development of CF101 for such other indications as follow: (i) $3 million upon marketing authorization in Japan for the second indication; and (ii) $1 million upon the commencement of each Phase III clinical trial in Japan for each indication after the first indication.

NOTE 12:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

In addition to the amounts detailed above, the Company will be entitled to royalties of 7%-12% on sales of the CF101 marketed by the Japanese Corporation according to the agreement and on additional revenues from sales of raw materials to the Japanese corporation for the purpose of the development, production and marketing of the CF101. If the Japanese corporation decides to produce the raw materials itself, the Company will be entitled to an additional $ 1 million (gross). Furthermore, according to the agreement, the Company will be entitled to receive additional amounts if the Japanese corporation requests information regarding the results of other clinical trials conducted by the Company in the future. The Company is committed to pay 5% of the above amounts as brokerage commission to a Japanese company which brokered the agreement. The agreement is for an indefinite period.

2. On December 22, 2008, the Company signed an agreement regarding the provision of a license for its CF101 drug with a South Korean pharmaceutical company, Kwang Dong Pharmaceutical Co. Ltd. (the "Korean License Agreement" and the "Korean Company", respectively). According to the license agreement, the Company granted the Korean Company a license to use, develop and market its CF101 drug for treating only rheumatoid arthritis only in the Republic of Korea.

   According to the license agreement, the Company is entitled to receive the following amounts:

   a) A non-refundable amount of $300 thousand that was received on the effective date of the license agreement in 2006, and up to $1.2 million (gross) based on the Company's achievement of certain milestones as follows: (i) $200 thousand upon the public announcement of the data from the Can-Fite Phase IIb clinical trial (such amount was received and included in the Company's revenue for the year ended December 31, 2010); (ii) $200 thousand upon commencement of the first clinical study by the Korean Company in the Republic of Korea; (iii) $200 thousand upon submission by the Korean Company of a new drug application in the Republic of Korea; (iv) $300 thousand upon all approval, licenses or authorizations of any regulatory authority necessary for the commercial marketing, sale and use of the product in the United States, in the European Union as a whole or in any one of the following countries: Germany, Italy, the United Kingdom, France or Switzerland; and (v) $300 thousand upon commercial launch of the product in the Republic of Korea.

   b) The Company is entitled to annual royalties of 7% based on sales of CF101 in Korea as marketed by the Korean Company according to the Korean License Agreement.

   As of December 31, 2014, the Company estimates that such contingent payments are remote.

NOTE 12:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

3. Lease commitments:

The Company leases motor vehicles through operating leases. The lease period ends in April 2017. Future minimum lease commitments under non-cancelable operating leases as of December 31, 2014 are as follows:

	NIS in thousands
2015	144
2016	59
2017	9
	212

Lease expenses for the years ended December 31, 2012, 2013 and 2014 were approximately NIS 246, NIS 229 and NIS 185, respectively.

NOTE 13:- EQUITY

a. Composition of share capital:

	December 31, 2014		December 31, 2013	
	Authorized	Issued and outstanding	Authorized	Issued and outstanding
	Number of Shares			
Ordinary shares of NIS 0.25 par value each	40,000,000	21,763,404	40,000,000	16,149,554

b. Issued and outstanding capital:

	Number of shares	NIS par value
Balance at December 31, 2012	10,935,196	2,733,799
Issuance of share capital	4,862,836	1,215,709
Exercise of warrants (Series 8, 10, 11)	2,940	735
Exercise of unlisted share options	348,582	87,146
Balance at December 31, 2013	16,149,554	4,037,389
Issuance of share capital	5,560,194	1,390,048
Issuance of shares - share based payment	52,000	13,000
Exercise of unlisted share options	1,656	414
Balance at December 31, 2014	21,763,404	5,440,851

c. Ordinary shares and rights attached to shares:

On May 2, 2013, the annual general meeting of the Company's shareholders approved a reverse stock split of one share for each twenty five shares outstanding (1:25) (the “Reverse Split”). The Reverse Split became effective as of the close of business on May 10, 2013. The Company's authorized share capital after the Reverse Split was NIS 10 million divided into 40 million ordinary shares, NIS 0.25 par value per share, of the Company. All ordinary shares, warrants, options, per share data and exercise prices included in these financial statements and notes for all periods presented have been retroactively adjusted to reflect the Reverse Split with respect to the Company’s share capital.

NOTE 13:- EQUITY (Cont.)

All ordinary shares have equal rights for all intent and purposes and each ordinary share confers its holder:

1. The right to be invited and participate in all the Company's general meetings, both annual and regular, and the right to one vote per ordinary share owned in all votes and in all Company's general meeting participated.

2. The right to receive dividends if and when declared and the right to receive bonus shares if and when distributed.

3. The right to participate in the distribution of the Company's assets upon liquidation.

4. Quoted on the Tel-Aviv Stock Exchange and New-York Stock Exchange.

d. Issue of shares and warrants and changes in equity:

1. On March 26, 2012, 23,333 warrants (Series 5) were exercised into 933 ordinary shares of the Company for a total consideration approximately NIS 76 thousand. The remaining 13,226,667 warrants (Series 5) which had not been exercised expired on March 31, 2012.

2. On May 1, 2012, the Company offered securities to the public according to a shelf proposal report which was published on the basis of a shelf prospectus which the Company published on May 27, 2010. The securities were offered to the public in 4,000 units at a minimum price of NIS 1,431 per unit. Each unit comprised of 120 ordinary shares at NIS 0.477 per share, 2,000 warrants (Series 8) and 3,000 warrants (Series 9) (both series of warrants at no consideration). Every 25 warrants (Series 8) were exercisable into one ordinary share, NIS 0.25 par value per share, of the Company in consideration of NIS 13.75, linked to the Israeli CPI with the base index being the CPI of March 2012. The exercise period of the warrants was until May 1, 2013. In addition, every 25 warrants (Series 9) is exercisable into one ordinary share of the Company in consideration of NIS 21.25, unlinked. The exercise period of the warrants is until May 1, 2015.

   Due to an oversubscription, 4,056 units were purchased at NIS 1,440 per unit for total proceeds of NIS 5,349 thousand (net of issue expenses of approximately NIS 491 thousand). The Series 8 warrants expired on December 31, 2013.

3. On February 5, 2013, the Company offered securities to the public according to a shelf proposal report which was published on the basis of a shelf prospectus which the Company published on July 26, 2012. The securities were offered to the public in 6,927 units at a minimum unit price of NIS 3,144 per unit. Each unit comprised of 400 ordinary shares of the Company at NIS 7.86 per share, 5,000 warrants (Series 10) and 5,000 warrants (Series 11). Every 25 warrants (Series 10) are exercisable into one ordinary share of the Company for NIS 9.85 linked to the Israeli consumer price index, The warrants are exercisable until October 31, 2015. In addition every 25 warrants (Series 11) are exercisable into one ordinary share, NIS 0.25 par value per share, of the Company for NIS 9.80, with the warrants being initially linked to the Israeli consumer price index for December 2012. The warrants are exercisable until April 30, 2016.

   Due to an oversubscription, 7,477 units were purchased at a price of NIS 3,544 per unit for total proceeds of NIS 23,926 thousand (net of issuance expenses of approximately NIS 2,572 thousand). The issuance proceeds were received on February 5, 2013. The shares included in the units were listed for trading on February 5, 2013.

NOTE 13:- EQUITY (Cont.)

As part of the February 5, 2013 financing, the Company's board of directors approved the grant to certain of the Company's external advisors of 1,682,000 warrants (Series 10) exercisable into 67,280 ordinary shares of the Company for an exercise price of NIS 0.394 per warrant. The warrants (Series 10) are exercisable until October 31, 2015. The grant was considered as additional issuance expenses related to the financing round. A total amount of NIS 125 thousand was recorded as capital reserve from share based payment.

On August 1, 2013 and August 4, 2013, a general meeting of the shareholders and the holders of warrants (Series 10 and Series 11), respectively, approved a settlement according to which the exercise price of such warrants (Series 10 and Series 11) will no longer be linked to the Israeli consumer price index. On August 20, 2013, the District Court in Lod, Israel approved such settlement. The settlement changes the classification of the warrants (Series 10 and Series 11) from liabilities to equity instruments, thereby increasing the Company's shareholders' equity, which in turn may be required to meet certain listing standards of certain U.S. national securities exchanges.

4. During 2013 8,714,576 unlisted options were exercised into 348,582 ordinary shares of the Company for a total consideration of approximately NIS 87 thousand.

5. On June 23, 2013, 6,000 warrants (Series 8) were exercised to purchase 240 ordinary shares, NIS 0.25 par value per share, of the Company for total consideration of approximately NIS 4 thousand.

6. On November 17, 2013, 30,000 warrants (Series 8) were exercised to purchase 1,200 ordinary shares, NIS 0.25 par value per share, of the Company for total consideration of approximately NIS 23 thousand.

7. On December 26, 2013, 25,000 warrants (Series 10) were exercised to purchase 1,000 ordinary shares, NIS 0.25 par value per share, of the Company for total consideration of approximately NIS 10 thousand.

8. On December 26, 2013, 12,500 warrants (Series 11) were exercised to purchase 500 ordinary shares, NIS 0.25 par value per share, of the Company for total consideration of approximately NIS 5 thousand.

9. On October 23, 2013, the Company offered securities to the public according to a shelf proposal report which was published on the basis of a shelf prospectus which the Company published on July 26, 2012. The securities were offered to the public in 3,600 units at the minimum unit price of NIS 5,000 thousand per unit. Each unit comprised of 500 ordinary shares at NIS 10 per share and 375 warrants (Series 12) for no additional consideration.

   Due to an oversubscription, 3,675 units were purchased at a price of NIS 5,800 per unit for total proceeds of NIS 20,138 thousands (net of issuance expenses of approximately NIS 1,177 thousands). The issuance proceeds were received on October 23, 2013. Until the use of issuance proceeds, the issuance proceeds are to be held in the Company's accounts and will be invested by it in accordance with the Company's investment policy as in place from time to time, provided that every aforesaid investment will be secure investments, including and without derogating from the generality of the aforesaid, a shekel interest bearing deposit account or foreign currency interest bearing deposit account. The shares included in the units were listed for trading on October 23, 2013.

NOTE 13:- EQUITY (Cont.)

On October 22, 2013, the Company's board of directors approved the grant to certain of the Company's external advisors of 91,875 warrants (Series 12) exercisable into 91,875 ordinary shares, NIS 0.25 par value per share, of the Company. The grant was included in the issuance expenses of the Company in connection with the financing round. The exercise price of the options is NIS 15.29 per option and the options are not linked to the Israeli Consumer Price Index. The warrants (Series 12) expire on October 22, 2016. A total amount of NIS 159 thousand was recorded as capital reserve from share based payment.

10. On November 2013 the Company's board of directors approved the private placement of 34,536 ordinary shares, NIS 0.25 par value per share, of the Company. Upon issuance, the proceeds of such private placement will be approximately $100 thousand, which represent a price of $2.90, or NIS 10.23, per ordinary share. Such price per share is equal to the closing price per share of the Company's ordinary shares on the TASE on November 3, 2013. The shares were listed for trading on the TASE on November 13, 2013.

11. In March 2014, the Company completed a private placement with certain institutional and accredited investors, pursuant to which it sold an aggregate of 982,344 ADSs representing 1,964,688 ordinary shares and warrants to purchase an additional 491,172 ADSs representing 982,344 ordinary shares for an aggregate purchase price of NIS 17,567 thousand (the "March 2014 Financing"). The warrants may be exercised at any time after September 10, 2014 for a period of four years from the date of issuance and have an exercise price of $6.43 per ADS (equivalent to $3.215 per ordinary share) (subject to certain adjustments). The issuance costs in relation to the March 2014 financing were NIS 1,795 thousand. The Company also issued placement agent warrants to purchase 49,117 ADSs representing 98,234 ordinary shares exercisable at $6.43 per ADS (equivalent to $3.215 per ordinary share) (subject to certain adjustments) for a period of four years. The placement agent warrants may be exercised on a cashless basis at any time after September 10, 2014 and contain registration rights covering the resale of the ordinary shares. The fair value of the placement agents warrants at the grant date was NIS 381 thousand and considered as additional issuance costs.

    In relation to the issuance of March 2014 Financing, the Company first allocated the proceeds to the warrant, that due to the dollar exercise price terms and in accordance with IAS 39 is being considered a freestanding liability instrument that is measured at fair value at each reporting date, based on its fair value, with changes in the fair values being recognized in the Company's statement of comprehensive loss as financial income or expense. The remaining proceeds were allocated to the shares and were recorded to equity. The issuance costs were allocated between the warrants and the shares in proportion to the allocation of the proceeds. The portions of the issuance costs that were allocated to the warrants and to the ordinary share were recorded as financial expense in the Company's statement of comprehensive loss and to the additional paid in capital in the Company's balance sheet, respectively.

    The fair value of the warrants at the commitment date and December 31, 2014 were NIS 3,812 thousand and NIS 1,654 thousand, respectively with changes recorded as financial income in the Company's statement of comprehensive loss.

NOTE 13:- EQUITY (Cont.)

12. In December 2014, the Company completed an at-the-market registered direct offering with certain institutional investors, pursuant to which it sold an aggregate of 1,797,753 ADSs representing 3,595,506 ordinary shares. In addition, the Company issued to the investors unregistered warrants to purchase 898,877 ADSs representing 1,797,753 ordinary shares. The offering (the "December 2014 Financing") resulted in gross proceeds of NIS 31,923 thousand. The warrants may be exercised for a period of five years from the date of issuance and have an exercise price of $4.45 per ADS (equivalent to $2.225 per ordinary share) (subject to certain adjustments). The issuance costs in relation to the December 2014 financing were NIS 3,020 thousand. The Company also issued placement agent warrants to purchase 89,888 ADS representing 179,775 ordinary shares exercisable at $4.45 per ADS (equivalent to $2.225 per ordinary share) (subject to certain adjustments) per share for a period five years. The placement agent warrants may be exercised on a cashless basis at any time after December 8, 2014 and contain registration rights covering the resale of the ordinary shares underlying the placement agent warrants. The fair value of the placement agents warrants at the grant date was NIS 613 thousand and considered as additional issuance costs.

    In relation to the issuance of December 2014 Financing, the Company first allocated the proceeds to the warrant, that due to the dollar exercise price terms and in accordance with IAS 39 is being considered a freestanding liability instrument that is measured at fair value at each reporting date, based on its fair value, with changes in the fair values being recognized in the Company's statement of comprehensive loss as financial income or expense. The remaining proceeds were allocated to the shares and were recorded to equity. The issuance costs were allocated between the warrants and the shares in proportion to the allocation of the proceeds. The portions of the issuance costs that were allocated to the warrants and to the ordinary share were recorded as financial expense in the Company's statement of comprehensive loss and to the additional paid in capital in the Company's balance sheet, respectively.

    The fair value of the warrants at the commitment date and December 31, 2014 were NIS 6,127 thousand and NIS 5,315 thousand, respectively with changes in recorded as financial income in the Company's statement of comprehensive loss.

13. During 2014, unlisted options were exercised into 1,656 ordinary shares of the Company for a total consideration of NIS 0.41 thousand.

e. Warrants classified as liability:

As of December 31, 2013, the Company had 9,907,500 registered warrants (Series 7) that were exercisable into 396,300 ordinary shares of the Company, in every trading day except from the 12th to the 16th of each calendar month from their admission to trading through November 16, 2013 for the exercise price of NIS 20 per share, linked to the Israeli CPI form October 2011. Since the exercise price is linked to the Israeli CPI, these warrants were classified as a liability in the Company's statements of financial position, remeasured at fair value each with changes recorded as financial income (loss) in the Company's statement of comprehensive loss.

NOTE 13:- EQUITY (Cont.)

On November 7, 2013 the Company filed an application with the District Court in Petach-Tikva, Israel to approve an extension of all warrants (Series 7) until March 31, 2014. On November 20, 2013, the District Court in Petach-Tikva, Israel approved the convening of a general meeting of the Company's shareholders and a meeting of the holders of warrants (Series 7) of the Company to approve the extension of the exercise period of the warrants (Series 7) until March 31, 2014. The meetings that convened on January 6, 2014 approved the extension and on January 27, 2014 the District Court in Petach-Tikva approved the extension until March 31, 2014.

On March 31, 2014, all warrants (Series 7) were expired. Accordingly, the Company recorded an amount of NIS 119 thousand as financial income in its statement of comprehensive loss.

As described at Note 13.d.11 and 12 above, in March and December 2014 the Company issued warrants to purchase 491,172 ADSs representing 982,334 ordinary shares and 898,877 ADSs representing 1,797,753 ordinary shares.

f. Warrants classified as equity:

The Company has 12,168,000 registered warrants (Series 9) that are exercisable into 486,720 ordinary shares of the Company for the exercise price of NIS 21.25 per share. These warrants are exercisable until May 1, 2015.

The Company has 39,042,000 registered warrants (Series 10) that are exercisable into 1,561,680 ordinary shares of the Company for NIS 9.85 per share. The warrants are exercisable until October 31, 2015.

The Company has 37,372,500 registered warrants (Series 11) that are exercisable into 1,494,900 ordinary shares of the Company for NIS 9.80 per share. The warrants are exercisable until April 30, 2016.

The Company has 1,470,000 registered warrants (Series 12) that are exercisable into 1,470,000 ordinary shares of the Company for NIS 15.29 per share. The warrants are exercisable until October 22, 2016.

As described at Note 13.d.11 and 12 above, in March and December 2014 the Company issued warrants to purchase 49,117 ADSs representing 98,324 ordinary shares and 89,888 ADSs representing 179,775 ordinary shares.

g. Unlisted share options:

On November 28, 2013, the Board of Directors approved the adoption of the 2013 ESOP (the "2013 Plan"). Under the 2013 Plan, the Company may grant its officers, directors, employees and consultants, Stock options, of the Company. Each Stock option granted shall be exercisable at such times and terms and conditions as the Board of Directors may specify in the applicable option agreement, provided that no option will be granted with a term in excess of 10 years.

Upon the adoption of the 2013 ESOP the Company reserved for issuance 1,000,000 shares of Common Stock, NIS 0.25 par value each.

On May 28, 2014 the Company’s board of directors approved the extension by one year of options which are exercisable into 502,025 ordinary shares of the Company, originally granted to investor on October 2010, till October 21, 2015. As of May 28, 2014, the modification date, the Company has evaluated the incremental fair value to be NIS 331 which was recorded as immediately expense.

NOTE 13:- EQUITY (Cont.)

h. Treasury shares:

As of December 31, 2014, the Company's shares held by OphthaliX amounted to 446,827 ordinary shares.

	December 31,	
	2014	2013
	%	
Percentage of issued capital	2.05	2.77

NOTE 14:-SHARE-BASED PAYMENT TRANSACTIONS

a. Expenses recognized in the financial statements:

	Year ended December 31,		
	2014	2013	2012
	NIS in thousand		
Research and development expenses	27	92	144
General and administrative expenses	799	2,622	1,312
	826	2,714	1,456

b. Share-based payment transactions granted by the Company:

1. On February 28, 2013, OphthaliX's board of directors approved the appointment of Barak Singer as its Chief Executive Officer, effective March 1, 2013. The board of directors also approved an amendment, dated February 28, 2013, to the existing employment agreement and non-competition agreement, dated February 22, 2011, pursuant to which he was to serve as Chief Executive Officer of OphthaliX while at the same time continuing to serve as Vice-President of Business Development of the Company. He was required to devote approximately 50% of his time to each position.

   On April 22, 2013, OphthaliX's board of directors approved the grant of options to Mr. Singer. In accordance with the option agreement, he received options to acquire 104,412 shares of common stock of OphthaliX at an exercise price of $5.29 (the “Time Based Options”) which expire ten years from the grant date. The Time Based Options provided for vesting over a period of three years on a quarterly basis over twelve consecutive quarters from the date of commencement of the employment of Mr. Singer. In addition, the Company's board of directors also approved the grant of an aggregate of 469,855 options to Mr. Singer, to acquire 104,412 shares of common stock of OphthaliX at an exercise price of $5.29 in accordance with the terms of the 2012 Plan, and which expire ten years from the grant date. These options provided for vesting upon the achievement of certain business and financial milestones, as defined in the agreement governing the same.

   On July 28, 2014, by mutual agreement, Mr. Singer ceased serving as OphthaliX Chief Executive Officer and as Vice-President of Business Development of Can-Fite. As of December 31, 2014 all his granted options were forfeited/expired.

NOTE 14:- SHARE-BASED PAYMENT TRANSACTIONS (Cont.)

According to IFRS 2 compensation cost initially is recognized based on an estimate of instruments expected to vest. Each reporting period a company must reevaluate its estimate of the number of instruments that ultimately will be forfeited if the requisite service has not been or is not expected to be provided. The effect of this change in estimated forfeitures is accounted for as a cumulative effect of a change in an accounting estimate in the period that the estimate is revised.

Based on the above accounting policy, for the year ended December 31, 2014 the Company reversed all previous compensation which related to the unvested option at amount of NIS 296.

2. On March 21, 2013, the Company's board of directors approved a grant of 740,000 unlisted options which are exercisable into 29,600 shares, NIS 0.25 par value per share, of the Company to two employees of the Company, three senior officers and three advisors. The exercise price of the options is NIS 0.326 per option. The options vest each quarter over a period of 48 months from the date of grant. According to the binomial model, the weighted average of the fair value of the options on the date of grant was NIS 0.204 per option and a total of NIS 141 thousand for all options, which is based on the following inputs: the closing price of the Company's shares of NIS 0.326, ranges of risk-free interest of 1.64%-6.86%, life of the options of 10 years, annual volatility range of 57.58%-72.10%, annual employee turnover of 5%, early exercise factor of 2-2.5 and distribution of annual dividend of 0%.

   The general manager of the Tel Aviv Stock Exchange ("TASE") approved the listing of the shares issuable upon the exercise of the options for trading on May 6, 2013.

3. On May 2, 2013, the annual general meeting of the Company's shareholders approved the grant to one of the Company's directors of 250,000 unlisted options which are exercisable into 10,000 ordinary shares, NIS 0.25 par value per share, of the Company. The exercise price of the options is NIS 0.6 per option. According to the binomial model, the economic value of the options on the date when the Company's board of directors approved the grant was NIS 0.148 per option and a total of NIS 36 thousand for all options, which is based on the following inputs: the closing price of the Company's shares of NIS 0.326, ranges of risk-free interest of 1.64%-6.86%, life of the options of 10 years, annual volatility range of 57.58%-72.10%, annual employee turnover of 5%, early exercise factor of 2.5 and distribution of annual dividend of 0%.

   The director was entitled to exercise half of such options immediately upon the date of the grant and the other half of the options become exercisable in equal amounts every quarter over a period of two years. On May 6, 2013, the general manager of the TASE approved the listing of the shares issuable upon the exercise of the options for trading.

4. On May 20, 2013, one of the advisors informed the Company that he waived the 80,000 unlisted options which were awarded to him on March 21, 2013 (see Note 14.b.2). The Company accounted for the waiver as a cancellation of the award and recorded an expense totaling NIS 23 thousands.

NOTE 14:- SHARE-BASED PAYMENT TRANSACTIONS (Cont.)

5. On May 9, 2013, the board of directors of OphthaliX granted options, which were modified on May 29, 2013 as to number and exercise price, to purchase 13,055 shares of its common stock to the Company's Chief Financial Officer. These options have an exercise price of $9.00 (as of December 31, 2014 NIS 35) per share and expire on May 29, 2023. 29,375 of these options vest immediately and the remaining 29,375 will vest over a period of three years on a quarterly basis for 12 consecutive quarters from the date of the grant. The Company accounted for the modification in accordance with IFRS 2, which measures the fair value of the replacement award against the fair value of the cancelled award on the cancellation date. During 2013 the Company recognized an expense of $62 (NIS 224) of which $38 (NIS 137) was related to the modification.

6. On May 9, 2013 the board of directors of OphthaliX approved the grant of options, with the same terms as the options granted to OphthaliX's Chief Financial Officer as described above, to certain members of OphthaliX's board of directors, Secretary and a director of EyeFite. The option grants to the Secretary and EyeFite director were made but later rescinded by the OphthaliX's board of directors on June 13, 2013 and the respective grantees waived any rights in and to such options. All unrecognized compensation costs were recorded on the cancellation date and amounted to $211 (NIS 762). The options to be granted to the members of the Company's board of directors, which also required the approval of the Company's stockholders, were never granted due to the failure to obtain such stockholders approval.

7. On July 1, 2013, the board of directors of OphthaliX approved the grant of options to purchase 52,222 shares of common stock of OphthaliX at $6.638 per share for a period of ten years to one of its directors. The options vest as follows: 1/12th vested on September 30, 2013 and 1/12th of the total options vest on the last day of each 11 quarters thereafter so long as he remains a director, until fully vested.

8. On January 30, 2014 one of the Company's directors ceased serving as a director and all her 350,000 granted options exercisable into 14,000 ordinary shares forfeited.

9. On April 1, 2014, the Company engaged an external advisor for investor relation services, pursuant to which the Company agreed to issue an aggregate of 26,000 ADS representing 52,000 ordinary shares as partial consideration. As of December 31, 2014 the Company recorded an amount of NIS 333 thousand for share based payment expenses relating to this transaction.

10. On July14, 2014, the Company's shareholders' meeting approved the grant of options to acquire up to 10,000 of the Company's ordinary shares to one of its directors at an exercise price of NIS 12 per share. The options will vest over a period of three years on a quarterly basis for 12 consecutive quarters from the date of the grant. The term of the options is 10 years.

NOTE 14:- SHARE-BASED PAYMENT TRANSACTIONS (Cont.)

c. Movement during the year:

The following table lists the number of share options, their weighted average exercise prices and modification in option plans of employees, directors and consultants for the periods indicated:

	Shares subject to options outstanding					
	2014		2013		2012	
	Number	Weighted average exercise price	Number	Weighted average exercise price	Number	Weighted average exercise price
		NIS		NIS		NIS
Outstanding at beginning of year	623,279	15.23	1,016,945	11.28	1,018,428	11.15
Grants	10,000	12.00	39,600	9.88	38,000	12.17
Exercised	(1,656)	0.25	(348,581)	0.25	(24,115)	7.27
Forfeited/expired	(38,916)	13.61	(84,685)	26.88	(15,368)	11.41
Outstanding at end of year	592,707	15.33	623,279	15.23	1,016,945	11.28
Exercisable at end of year	565,694	15.58	581,833	15.57	986,402	11.24

d. The weighted average remaining contractual life for the shares subject to options outstanding as of December 31, 2014, 2013 and 2012 was 3.11 years, 4.43 years and 4.01 years, respectively.

e. The range of exercise prices for shares subject to options outstanding as of December 31, 2014, 2013 and 2012 was between NIS 0.25 and NIS 31.175.

f. The fair value of the Company's share options granted for the years ended December 31, 2013 and 2014 was estimated using the Binomial option pricing model using the following assumptions:

	December 31,	
Description	2014	2013
Risk-free interest rate	1.29%	1.64%-6.86%
Expected volatility	56.68%	57.58%-72.10%
Dividend yield	0	0
Contractual life	10	10
Early Exercise Multiple (Suboptimal Factor)	2.5	2-2.5
Weighted average share price	1.701	4.608

NOTE 15:- RESEARCH AND DEVELOPMENT EXPENSES

	Year ended December 31,		
	2014	2013	2012
	NIS in thousands		
Clinical and preclinical trials	12,295	11,850	9,623
Salary and related expenses	1,931	1,705	1,529
Patents	760	717	1,130
Royalties	510	606	240
Laboratory materials	205	98	146
Rent	184	188	216
Depreciation	9	8	30
Others	306	218	246
	16,200	15,390	13,160

NOTE 16:- GENERAL AND ADMINISTRATIVE EXPENSES

	Year ended December 31,		
	2014	2013	2012
	NIS in thousands		
Professional services	3,420	5,776	3,356
Investors and public relations	3,069	3,281	435
Salary and related expenses	2,089	3,777	2,104
Directors' fee	691	914	1,539
Rent	123	123	165
Travel	850	650	381
Insurance	465	388	410
Stock exchange fees	317	361	126
Office and computer maintenance	258	284	393
Vehicle maintenance	89	135	110
Depreciation	35	49	56
Others	167	184	197
	11,573	15,922	9,272

NOTE 17:- FINANCE EXPENSES (INCOME)

	Year ended December 31,		
	2014	2013	2012
	NIS in thousands		
Finance expenses:			
Bank commissions	58	56	27
Issuance expenses related to warrants exercisable into shares	1,170	651	32
Net loss from exchange rate fluctuations	-	185	-
	1,228	892	59
Finance income:			
Interest income on bank deposits	(45)	(92)	(50)
Net gain from exchange rate fluctuations	(1,366)	-	(94)
Net change in fair value warrants exercisable into shares	(3,089)	(1,309)	(429)
	(4,500)	(1,401)	(573)

NOTE 18:- LOSS PER SHARE

a. Details of the number of shares and loss used in the computation of loss per share:

	Year ended December 31,					
	2014		2013		2012	
	Weighted number of shares	Loss	Weighted number of shares	Loss	Weighted number of shares	Loss
	In thousands	NIS in thousands	In thousands	NIS in thousands	In thousands	NIS in thousands
Number of shares and loss used in the computation of basic and diluted loss per share	17,546	23,759	13,712	29,049	10,051	20,862

b. To compute diluted loss per share for the year ended December 31, 2014, the total number of 8,071,406 shares subject to outstanding warrants and 1,094,736 shares subject to outstanding unlisted options have not been taken into account since they have anti-dilutive effect.

NOTE 19:- TAXES ON INCOME

a. Corporate tax rates:

1. Israeli taxation:

The Israeli corporate tax rate is 25% in 2012 - 2013 and 26.5% in 2014.

On July 30, 2013, the Israeli Parliament approved the second and third readings of the Economic Plan for 2013-2014 ("Amended Budget Law") which consists, among others, of fiscal changes whose main aim is to enhance the collection of taxes in those years. These changes include, among others, raising the Israeli corporate tax rate from 25% to 26.5% effective from January 1, 2014.

2. Income tax on non-Israeli subsidiary:

The corporate tax in the U.S. applying to a Company's subsidiary (incorporated in state of Delaware), consists of a progressive corporate tax at a rate of up to 35% plus state tax and local tax at rates depending on the state and the city in which the company's subsidiary manages its business. In the Company's estimation, it is subject to approximately a 40% tax rate.

b. Final tax assessments:

The Company received final tax assessments through 2010.

The related company, OphthaliX and Eye-Fite, has not received final tax assessments since its incorporation.

c. Net operating carryforward losses for tax purposes and other temporary differences:

As of December 31, 2014, the Company and Eyefite had carryforward losses amounting to approximately NIS 272,612 thousand and NIS 9,814 thousand.

Ophthalix is subject to U.S. income taxes. As of December 31, 2014, the Company has net operating loss carryforwards for federal income tax purposes of approximately $1,503 thousand (approximately NIS 5,845 thousand) which will expire in the years 2018 to 2034. The Company has no operating loss carry forwards for state income tax purposes.

c. Deferred taxes

The Company did not recognize deferred tax assets for carryforward losses and other temporary differences because their utilization in the foreseeable future is not probable.

d. Theoretical tax:

The reconciliation between the tax expense, assuming that all the income and expenses, gains and losses in the statement of income were taxed at the statutory tax rate and the taxes on income recorded in statement of comprehensive loss, does not provide significant information and therefore was not presented.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20:- TRANSACTIONS WITH RELATED PARTIES

	Year ended December 31,		
	2014	2013	2012
	NIS in thousands		
Management and consulting fees (including bonuses) (1)	1,312	1,050	1,050
Other expenses and share-based payment (1)	57	71	318
Patent expenses	793	677	1,093
Directors' fee and share-based payment (2)	417	387	646
(1) Number of related parties	1	1	1
(2) Number of directors	4	3	6

NOTE 21:- SUBSEQUENT EVENTS

1. In March 2015, the Company issued a financial support letter pursuant to which the Company committed to cover any shortfall in OphthaliX's costs and expenses of the operations which are in excess of its available cash to finance its operations, including cash generated from any future sale of Can-Fite shares held by OphthaliX. The letter remains in effect for a period of at least 14 months from March 2015 and any related balance bears interest at a rate of 3% per annum.

2. On March 19, 2015, the Company's board of directors approved a grant of unlisted options exercisable into 40,000 of the Company's ordinary shares to three of its employees and one senior officer for an exercise price of NIS 8.118 per shares. The options will vest on a quarterly basis for a period of 48 months from the grant date.

3. On March 20, 2015, the Company entered into a Distribution and Supply Agreement with Cipher Pharmaceuticals ("Cipher") granting Cipher the exclusive right to distribute CF101 in Canada for the treatment of psoriasis and RA.

   Under the Distribution and Supply Agreement, the Company is entitled to CDN$1.65 million upon execution of the agreement plus milestone payments upon receipt of regulatory approval by Health Canada for CF101 and the first delivery of commercial launch quantities as follows (i) CDN$1 million upon the first approved indication for either psoriasis or RA, and (ii) CDN $1 million upon the second approved indication for either psoriasis or RA. In addition, following regulatory approval, the Company shall be entitled to a royalty of 16.5% of net sales of CF101 in Canada and reimbursement for the cost of manufacturing CF101. The Company is also entitled to a royalty payment for any authorized generic of CF101 that Cipher distributes in Canada.

   The Company is responsible for supplying Cipher with finished product for distribution and conducting product development activities while Cipher is responsible for distribution, marketing and obtaining applicable regulatory approvals in Canada. The Distribution and Supply Agreement has an initial term of fifteen years, automatically renewable for additional five year periods and may be terminated in certain limited circumstances including certain breaches of the agreement and failure to achieve certain minimum quantities of sales during the contract period.

   The timeline to regulatory submissions to Health Canada will be determined by the completion of the remaining clinical trial program.

ITEM 19. Exhibits

Index to Exhibits

Exhibit No.	Description
1.1	Amended and Restated Articles of Association of Can-Fite BioPharma Ltd (1)
2.1	Form of Amended and Restated Deposit Agreement, by and among Can-Fite BioPharma Ltd., The Bank of New York Mellon and the Owners and Holders of American Depositary Shares, dated September 11, 2013 (2)
4.1	Employment and Non-Competition Agreement with Barak Singer, dated February 22, 2011 (effective March 20, 2011) (3)
4.2	Amendment to Employment and Non-Competition Agreement with Barak Singer, dated February 28, 2013 (3)
4.3	Employment and Non-Competition Agreement with Motti Farbstein, dated June 10, 2003 (3)
4.4	Consulting Agreement with BioStrategics Consulting, Ltd, dated September 27, 2005 (3)
4.5	Service Management Agreement with F.D. Consulting International and Marketing Ltd., dated June 27, 2002 (3)
4.6	Master Services Agreement with Accellient Partners, dated May 10, 2010 (3)
4.7	Patent License Agreement—*Exclusive*, by and between the U.S. Public Health Service and Can-Fite BioPharma Ltd., dated January 29, 2003 (3)
4.8	First Amendment to Exclusive Patent License Agreement L-249-2001/0, by and between the National Institutes of Health and Can-Fite BioPharma Ltd., dated August 15, 2005 (3)
4.9	Second Amendment to L-249-2001/0, by and between the National Institutes of Health and Can-Fite BioPharma Ltd., dated February 4, 2013 (3)
4.10	License Agreement, by and between The University of Leiden and Can-Fite BioPharma Ltd., dated November 2, 2009 (3)
4.11	License Agreement, by and between Seikagaku Corporation and Can-Fite BioPharma Ltd., dated September 22, 2006 (3)
4.12	Addendum to License Agreement, by and between Seikagaku Corporation and Can-Fite BioPharma Ltd., dated December 11, 2006 (3)
4.13	Representative Agreement, by and between Fuji Techno Interface Ltd. and Can-Fite BioPharma Ltd., dated September 22, 2006 (3)
4.14	Letter Agreement, by and between Seikagaku Corporation and Can-Fite BioPharma Ltd., dated December 8, 2009 (3)
4.15	License Agreement, by and between Kwang Dong Pharmaceutical Co., Ltd. and Can-Fite BioPharma Ltd., dated December 14, 2008 (3)
4.16	License Agreement, by and between Eye-Fite, Ltd. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.17	Services Agreement, by and among Denali Concrete Management Inc., Eye-Fite Ltd. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.18	Letter from Can-Fite BioPharma Ltd. to OphthaliX, Inc. regarding “Reimbursement for the Costs of the Clinical Trial”, dated February 24, 2013 (3)
4.19	Agreement, by and between Denali Concrete Management Inc. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)

Exhibit No.	Description
4.20	Stock Purchase Agreement, by and between Denali Concrete Management Inc. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.21	Subscription Agreement, by and between Denali Concrete Management Inc. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.22	Subscription Agreement, by and between Denali Concrete Management Inc. and Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.23	Common Stock Purchase Warrant issued by Denali Concrete Management Inc. to Can-Fite BioPharma Ltd., dated November 21, 2011 (3)
4.24	Can-Fite BioPharma Ltd. 2003 Israeli Share Option Plan (3)
4.25	Can-Fite BioPharma Ltd. 2013 Israeli Share Option Plan*
4.26	Form of Securities Purchase Agreement dated as of March 10, 2014 between Can-Fite BioPharma Ltd. and the investors listed therein (4)
4.27	Form of Warrant dated March 10, 2014 issued by Can-Fite BioPharma Ltd. (4)
4.28	Form of Registration Rights Agreement dated as of March 10, 20142014 between Can-Fite BioPharma Ltd. and the investors listed therein (4)
4.29	Form of Lock-Up Agreement dated March 10, 2014 between Can-Fite BioPharma Ltd. and officers and directors of Can-Fite Biopharma Ltd. (4)
4.30	Form of Placement Agent Warrant dated March 10, 2014 issued by Can-Fite BioPharma Ltd. to Roth Capital Partners, LLC(4)
4.31	Form of Securities Purchase Agreement dated as of December 2, 2014 between Can-Fite BioPharma Ltd. And the investors listed therein (5)
4.32	Form of Warrant issued by Can-Fite BioPharma Ltd. (5)
4.33	Letter Agreement between H.C. Wainwright & Co., LLC and Can-Fite BioPharma Ltd. dated December 2, 2014 (5)
4.34	Distribution and Supply Agreement between Can-Fite BioPharma Ltd. and Cipher Pharmaceuticals Inc. dated as of March 20, 2015*†
8.1	List of Subsidiaries of Can-Fite BioPharma Ltd. *
12.1	Certification by Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*
12.2	Certification by Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*
13.1	Certification by Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
13.2	Certification by Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
15.1	Consent of Independent Registered Public Accounting Firm.*

* File Herewith.

† Certain confidential information contained in this exhibit was omitted by means of redacting a portion of the text and replacing it with [...]. This exhibit has been filed separately with the Commission without the redaction pursuant to a Confidential Treatment Request under Rule 24b-2 of the Securities Exchange Act of 1934 and Rule 406 of the Securities Act.

(1) Incorporated herein by reference to Annual Report on 20-F filed with the SEC on March 31, 2014.

(2) Incorporated herein by reference to the Registration Statement on Form 8-A filed with the SEC on November 15, 2013.

(3) Incorporated herein by reference to Amendment No. 1 to the Draft Registration Statement on Form 20-F filed with the SEC on September 10, 2013.

(4) Incorporated herein by reference to the Current Report on Form 6-K filed with the SEC on March 10, 2014.

(5) Incorporated herein by reference to the Current Report on Form 6-K filed with the SEC on December 4, 2014.

SIGNATURES

The Registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this Annual Report on its behalf.

CAN-FITE BIOPHARMA LTD.

By: /s/ Pnina Fishman, Ph.D.
Pnina Fishman, Ph.D.
Chief Executive Officer

Date: March 27, 2015

Exhibit 4.25

Can Fite Biopharma LTD.

THE 2013 GLOBAL INCENTIVE OPTION SCHEME

DEFINITIONS

For purposes of the Global Incentive Option Scheme and related documents, including without limited, the Grant Notification Letter, the following definitions shall apply:

(a) **"Board" -** the Board of Directors of the Company.

(b) **"Cause"** — any of the following:

(i) conviction of any felony involving moral turpitude or affecting the Company or any of its affiliates;

(ii) any refusal to carry out a reasonable directive of the chief executive officer, the Board or the Grantee's direct supervisor, which involves the business of the Company or any of its affiliates and was capable of being lawfully performed;

(iii) embezzlement of funds of the Company or any of its affiliates;

(iv) any breach of the Grantee's fiduciary duties or duties of care of the Company or any of its affiliates; including without limitation disclosure of confidential information of the Company or any of its affiliates;

(v) any conduct (other than conduct in good faith), including without limitation, any act or omission, reasonably determined by the Board to be materially detrimental to the Company or any of its affiliates; and/or

(vi) if and as such term is or may be defined under the Grantee's employment agreement, service agreement or any other engagement agreement with the Company or any of its affiliates; and/or

(vii) should circumstances arise as a result of which the Grantees' employment with the Company and/or any of its affiliates is or may be terminated without severance pay.

For the avoidance of any doubt, it is hereby clarified that in any event of conflict between the definition of the term "Cause" in this Scheme and the definition of the term "Cause" in a certain employment agreement, the definition in this Scheme shall prevail in connection with the Option, with the Grant Notification Letter and with this Scheme.

(c) **"Chairman" -** the chairman of the Committee.

(d) **"Committee"** - a compensation committee appointed by the Board, which shall consist of no fewer than two members of the Board.

(e) **"Company"** —Can Fite Biopharma Ltd., an Israeli company.

(f) **"Date of Grant" -** the date of grant of an Option, as determined by the Board or the Committee and set forth in the Grantee's Grant Notification Letter.

(g) **"Employee"** - a person who is employed by the Company or any affiliate.

(h) **"Expiration Date" -** the date upon which an Option shall expire, as set forth in Section 7.2 of the Scheme.

(i) **"Fair Market Value"** - as of any date, the value of a Share determined as follows:

(i) If the Shares are listed on any established Share exchange or a national market system, including without limitation the Tel-Aviv Share Exchange, the NYSE MKT system, the NASDAQ National Market system, or the NASDAQ SmallCap Market of the NASDAQ Share Market, the Fair Market Value shall be the closing sales price for such Shares (or the closing bid, if no sales were reported), as quoted on such exchange or system for the last market trading day prior to time of determination, as reported in the Wall Street Journal, or such other source as the Board deems reliable;

(ii) If the Shares are regularly quoted by a recognized securities dealer but selling prices are not reported, the Fair Market Value shall be the mean between the high bid and low asked prices for the Shares on the last market trading day prior to the day of determination, or;

(iii) In the absence of an established market for the Shares, the Fair Market Value thereof shall be determined in good faith by the Board.

(j) **"Grantee"** - a person who receives or holds an Option under the Scheme.

(k) **"Grant Notification Letter"** - a document to be signed between the Company and a Grantee that sets out and inform the Grantee with respect to the terms and conditions of the grant of an Option.

(l) **"Non-Employee"** - a director, consultant, advisor, service provider of the Company or any affiliate, or any other person who is not an Employee.

(m) **"Option"** - an option to purchase one or more Shares of the Company pursuant to the Scheme.

(n) **"Purchase Price"** - the price for each Share subject to an Option.

(o) **"Scheme"** - this 2013 Global Incentive Option Scheme.

(p) **"Share"** - the ordinary shares, NIS 0.25 par value each, of the Company.

(q) **"Successor Company"** - any entity the Company is merged to or is acquired by, in which the Company is not the surviving entity.

(r) **"Transaction" —**

(i) Merger, acquisition or reorganization of the Company with one or more other entities in which the Company is not the surviving entity;

(ii) A sale of all or substantially all of the assets of the Company.

(s) **"Vested Option"** - any Option, which has already been vested according to the Vesting Dates.

(t) **"Vesting Dates"** - as determined by the Board or by the Committee, the date as of which the Grantee shall be entitled to exercise the Options or part of the Options, as set forth in Section 10 of the Scheme and in the Grantee's Grant Notification Letter.

THE SCHEME

This scheme, as amended from time to time, shall be known as Can Fite Biopharma Ltd. 2011 Global Incentive Option Scheme.

1. PURPOSE OF THE SCHEME

The Scheme is intended to provide an incentive to retain, in the employ of the Company and its affiliates, persons of training, experience, and ability, to attract new employees, directors, consultants, service providers and any other entity which the Board shall decide their services are considered valuable to the Company, to encourage the sense of proprietorship of such persons, and to stimulate the active interest of such persons in the development and financial success of the Company by providing them with opportunities to purchase shares in the Company, pursuant to the Scheme.

Incentives under the Scheme shall only be issued to Grantees subject to the applicable law in their respective country of residence for tax purposes or any other purposes, as the case may be.

2. ADMINISTRATION OF THE SCHEME

2.1 The Board shall have the power to administer the Scheme either directly or upon the recommendation of the Committee, all as provided by applicable law and in the Company's Articles of Association. Notwithstanding the above, the Board shall automatically have residual authority if no Committee shall be constituted or if such Committee shall cease to operate for any reason.

2.2 The Committee shall select one of its members as its Chairman and shall hold its meetings at such times and places as the Chairman shall determine. The Committee shall keep records of its meetings and shall make such rules and regulations for the conduct of its business as it shall deem advisable.

2.3 The Board and/or the Committee, if applicable subject to the approval of the Board, to the extent required under applicable law (and subject further to applicable laws) shall have the full power and authority to:

(i) designate participants;

(ii) determine the terms and provisions of the respective Grant Notification Letters, including, but not limited to, the number of Options to be granted to each Grantee, the number of Shares to be covered by each Option, provisions concerning the time and the extent to which the Options may be exercised and the nature and duration of restrictions as to the transferability or restrictions constituting substantial risk of forfeiture and to cancel or suspend awards, as necessary;

(iii) determine the Fair Market Value of the Shares covered by each Option;

(iv) designate the type of Options; alter any restrictions and conditions of any Options or Shares subject to any Options;

(v) alter any restrictions and conditions of any Options or Shares subject to any Options;

(vi) interpret the provisions and supervise the administration of the Scheme;

(vii) accelerate the right of a Grantee to exercise in whole or in part, any previously granted Option;

(viii) determine the Purchase Price of the Option;

(ix) prescribe, amend and rescind rules and regulations relating to the Scheme; and

(x) make all other deteuninations deemed necessary or advisable for the administration of the Scheme.

2.4 The Board or the Committee shall have the authority to grant, at its discretion, to the holder of an outstanding Option, in exchange for the surrender and cancellation of such Option, a new Option having a purchase price equal to, lower than or higher than the Purchase Price of the original Option so surrendered and canceled and containing such other terms and conditions, or to change the Purchase Price as the Board or the Committee may prescribe in accordance with the provisions of the Scheme.

2.5 Subject to the Company's Articles of Association, all decisions and selections made by the Board or the Committee pursuant to the provisions of the Scheme shall be made by a majority of its members except that no member of the Board or the Committee shall vote on, or be counted for quorum purposes, with respect to any proposed action of the Board or the Committee relating to any Option to be granted to that member. Any decision reduced to writing shall be executed in accordance with the provisions of the Company's Articles of Association, as the same may be in effect from time to time.

2.6 The interpretation and construction by the Committee of any provision of the Scheme or of any Grant Notification Letter there under shall be final and conclusive unless otherwise determined by the Board.

2.7 Subject to the Company's Articles of Association and the Company's decision, and to all approvals legally required, including, but not limited to the provisions of any applicable law, each member of the Board or the Committee shall be indemnified and held harmless by the Company against any cost or expense (including counsel fees) reasonably incurred by him, or any liability (including any sum paid in settlement of a claim with the approval of the Company) arising out of any act or omission to act in connection with the Scheme unless arising out of such member's own fraud or bad faith, to the extent peitnitted by applicable law. Such indemnification shall be in addition to any rights of indemnification the member may have as a director or otherwise under the Company's Articles of Association, any agreement, any vote of shareholders or disinterested directors, insurance policy or otherwise.

3. DESIGNATION OF PARTICIPANTS

The persons eligible for participation in the Scheme as Grantees shall include any Employees and/or Non-Employees of the Company or of any affiliate.

The grant of an Option hereunder shall neither entitle the Grantee to participate nor disqualify the Grantee from participating in, any other grant of Options pursuant to the Scheme or any other option or share plan of the Company or any of its affiliates.

4. SHARES RESERVED FOR THE SCHEME; RESTRICTION THEREON

4.1 The Company has reserved 966,634 authorized but unissued Shares, for the purposes of the Scheme and for the purposes of any other share option plans which may be adopted by the Company in the future, subject to adjustment as set forth in Section 6 below. Any Shares which remain unissued and which are not subject to the outstanding Options at the termination of the Scheme shall cease to be reserved for the purpose of the Scheme, but until termination of the Scheme the Company shall at all times reserve sufficient number of Shares to meet the requirements of the Scheme. Should any Option for any reason expire or be canceled prior to its exercise or relinquishment in full, the Shares subject to such Option may again be subjected to an Option under the Scheme or under the Company's other share option plans.

4.2 Each Option granted pursuant to the Scheme, shall be evidenced by a written Grant Notification Letter between the Company and the Grantee, in such foful as the Board or the Committee shall from time to time approve. Each Grant Notification Letter shall state, among other matters, the number of Shares to which the Option relates, the type of Option granted thereunder, the Vesting Dates, the Purchase Price per share, the Expiration Date and such other terms and conditions as the Committee or the Board in its discretion may prescribe, provided that they are consistent with this Scheme.

5. PURCHASE PRICE

5.1 The Purchase Price of each Share subject to an Option shall be determined by the Committee in its sole and absolute discretion in accordance with applicable law, subject to any guidelines as may be determined by the Board from time to time. Each Grant Notification Letter will contain the Purchase Price determined for each Grantee.

5.2 Without derogating from the above and in addition thereto, the Purchase Price of each Share subject to an Option shall be payable upon the exercise of an Option in the following acceptable forms of payment:

(i) cash, check or wire transfer;

(ii) at the discretion of the Committee, through delivery of Share (including other Share subject to the Options being exercised) having a Fair Market Value equal as of the date of exercise to the Purchase Price of the Share purchased and acquired upon the exercise of the Option, or by a different foun of cashless exercise method through a third party broker as approved by the Committee;

(iii) at the discretion of the Committee, any combination of the methods of payment permitted by any paragraph of this Section 5.2.

5.3 The Purchase Price shall be denominated in the currency of the primary economic environment of, either the Company or the Grantee (that is the functional currency of the Company or the currency in which the Grantee is paid) as determined by the Company.

6 . ADJUSTMENTS

Upon the occurrence of any of the following described events, Grantee's rights to purchase Shares under the Scheme shall be adjusted as hereafter provided:

6.1 In the event of Transaction, the unexercised Options then outstanding under the Scheme shall be assumed or substituted for an appropriate number of shares of each class of shares or other securities of the Successor Company (or a parent or subsidiary of the Successor Company) as were distributed to the shareholders of the Company in connection and with respect to the Transaction. In the case of such assumption and/or substitution of Options, appropriate adjustments shall be made to the Purchase Price so as to reflect such action and all other terms and conditions of the Grant Notification Letters shall remain unchanged, including but not limited to the vesting schedule, all subject to the deteunination of the Committee or the Board, which determination shall be in their sole discretion and final. The Company shall notify the Grantee of the Transaction in such form and method as it deems applicable at least 7 days prior to the effective date of such Transaction.

6.2 Notwithstanding the above and subject to any applicable law, the Board or the Committee shall have full power and authority to determine that in certain Grant Notification Letters there shall be a clause instructing that, if in any such Transaction as described in Section 6.1 above, the Successor Company (or parent or subsidiary of the Successor Company) does not agree to assume or substitute for the Options, the Vesting Dates shall be accelerated so that any unvested Option or any portion thereof shall be immediately vested as of the date which is 7 days prior to the effective date of the Transaction.

6.3 For the purposes of Section 6.1 above, an Option shall be considered assumed or substituted if, following the Transaction, the Option confers the right to purchase or receive, for each Share underlying an Option immediately prior to the Transaction, the consideration (whether shares, options, cash, or other securities or property) received in the Transaction by holders of shares held on the effective date of the Transaction (and if such holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares); provided, however, that if such consideration received in the Transaction is not solely ordinary shares (or their equivalent) of the Successor Company or its parent or subsidiary, the Committee may, with the consent of the Successor Company, provide for the consideration to be received upon the exercise of the Option to be solely ordinary shares (or their equivalent) of the Successor Company or its parent or subsidiary equal in Fair Market Value to the per Share consideration received by holders of a majority of the outstanding shares in the Transaction; and provided further that the Committee may determine, in its discretion, that in lieu of such assumption or substitution of Options for options of the Successor Company or its parent or subsidiary, such Options will be substituted for any other type of asset or property including cash which is fair under the circumstances.

6.4 The Board or the Committee shall have full power and authority to determine that in certain Grant Notification Letters there shall be a clause instructing that, if the Company is voluntarily liquidated or dissolved while unexercised Options remain outstanding under the Scheme, the Company shall immediately notify all unexercised Option holders of such liquidation, and the Option holders shall then have 7 days to exercise any unexercised Vested Option held by them at that time, in accordance with the exercise procedure set forth herein. Upon the expiration of such 7 days period, all remaining outstanding Options will terminate immediately.

6.5 If the outstanding shares of the Company shall at any time be changed or exchanged by declaration of a cash dividend, share dividend (bonus shares), distribution of subscription rights, share split, combination or exchange of shares, recapitalization, spin-off or any other like event by or of the Company, and as often as the same shall occur, then the number, class and kind of the Shares subject to the Scheme or subject to any Options therefore granted, and the Purchase Prices, shall be appropriately and equitably adjusted so as to maintain the proportionate number of Shares without changing the aggregate Purchase Price. Upon happening of any of the foregoing, the class and aggregate number of Shares issuable pursuant to the Scheme (as set forth in Section 6 hereof), in respect of which Options have not yet been exercised, shall be appropriately adjusted, all as will be determined by the Board whose determination shall be final.

7. TERM AND EXERCISE OF OPTIONS

7.1 Options shall be exercised by the Grantee by giving written notice to the Company and/or to any third party designated by the Company (the: "**Representative**"), in such form and method as may be determined by the Company, which exercise shall be effective upon receipt of such notice by the Company and/or the Representative and the payment of the Purchase Price at the Company's or the Representative's principal office. The notice shall specify the number of Shares with respect to which the Option is being exercised.

7.2 Options, to the extent not previously exercised, shall terminate forthwith upon the earlier of: (i) the date set forth in the Grant Notification Letter; (ii) the expiration of any extended period in any of the events set forth in Section 7.5 below, or (iii) ten (10) years from their Date of Grant.

7.3 The Options may be exercised by the Grantee in whole at any time or in part from time to time, to the extent that the Options become vested and exercisable, prior to the Expiration Date, and provided that, subject to the provisions of Section 7.5 below, the Grantee is employed by or providing services to the Company or any of its affiliates, at all times during the period beginning with the granting of the Option and ending upon the date of exercise.

7.4 Subject to the provisions of Section 7.5 below, in the event of termination of Grantee's employment or services, with the Company or any of its affiliates, all Options granted to such Grantee will immediately expire. A notice of termination of employment or service shall be deemed to constitute termination of employment or service. For the avoidance of doubt, in case of such termination of employment or service, the unvested portion of the Grantee's Option shall not vest and shall not become exercisable and the Grantee shall have no claim against the Company and/or its affiliate that his/her Options were prevented from continuing to vest as of such termination. Notwithstanding anything to the contrary mentioned above, a Grantee shall not cease to be an Employee only due to the transfer of such Employee's employment among the Company and its affiliates.

7.5 Notwithstanding anything to the contrary hereinabove and unless otherwise determined in the Grantee's Grant Notification Letter, an Option may be exercised after the date of termination of Grantee's employment or service with the Company or any affiliates during an additional period of time beyond the date of such termination, but only with respect to the number of Vested Options at the time of such termination according to the Vesting Dates, if:

(i) termination is without Cause, in which event any Vested Option still in force and unexpired may be exercised within a period of ninety (90) days after the date of such termination; or-

(ii) termination is the result of death or disability of the Grantee, in which event any Vested Option still in force and unexpired may be exercised within a period of twelve (12) months after the date of such termination; or -

(iii) prior to the date of such termination, the Committee shall authorize an extension of the terms of all or part of the Vested Options beyond the date of such termination for a period not to exceed the period during which the Options by their terms would otherwise have been exercisable.

For avoidance of any doubt, if termination of employment or service is for Cause, any outstanding unexercised Option (whether vested or non-vested), will immediately expire and terminate, and the Grantee shall not have any right in connection to such outstanding Options.

7.6 Any form of Grant Notification Letter authorized by the Scheme may contain such other provisions as the Committee may, from time to time, deem advisable.

7.7 The Options and any underlying Shares are extraordinary, one-time benefits granted to the Grantee and are not and shall not be deemed a salary component for any purpose whatsoever, including in connection with calculating severance compensation under applicable law.

7.8 Neither the Grantee nor any other person, as the case may be, shall have any claim to be granted any Options, and there is no obligation by the Company for uniformity of treatment of Grantees or their beneficiaries (if applicable). The terms and conditions of the Options granted under this Scheme and any of the Board's determinations and interpretations with respect thereto need not be the same with respect to each Grantee

(whether or not such Grantees are similarly situated).

8. VESTING OF OPTIONS

8.1 Subject to the provisions of the Scheme, each Option shall vest following the Vesting Dates and for the number of Shares as shall be provided in the Grant Notification Letter. However, no Option shall be exercisable after the Expiration Date.

8.2 An Option may be subject to such other terms and conditions on the time or times when it may be exercised, as the Committee may deem appropriate. The vesting provisions of individual Options may vary.

9. DIVIDENDS

With respect to all Shares (but excluding, for avoidance of any doubt, any unexercised Options) allocated or issued upon the exercise of Options purchased by the Grantee and held by the Grantee or by the Trustee, as the case may be, the Grantee shall be entitled to receive dividends in accordance with the quantity of such Shares, subject to the provisions of the Company's Articles of Association (and all amendments thereto) and subject to any applicable taxation on distribution of dividends.

10. PURCHASE FOR INVESTMENT

The Company's obligation to issue or allocate Shares upon exercise of an Option granted under the Scheme is expressly conditioned upon:

(i) the Company's completion of any registration or other qualifications of such Shares under all applicable laws, rules and regulations, or;
(ii) representations and undertakings by the Grantee (or his legal representative, heir or legatee, in the event of the Grantee's death) to assure that the sale of the Shares complies with any registration exemption requirements which the Company in its sole discretion shall deem necessary or advisable.

Such required representations and undertakings may include representations and agreements that such Grantee (or his legal representative, heir, or legatee):

(i) is purchasing such Shares for investment and not with any present intention of selling or otherwise disposing thereof; and;
(ii) agrees to have placed upon the face and reverse of any certificates evidencing such Shares a legend setting forth (a) any representations and undertakings which such Grantee has given to the Company or a reference thereto, and (b) that, prior to effecting any sale or other disposition of any such Shares, the Grantee must furnish to the Company an opinion of counsel, satisfactory to the Company, that such sale or disposition will not violate the applicable laws, rules and regulations of the United States or any other state having jurisdiction over the Company and the Grantee.

11. RESTRICTIONS ON ASSIGNABILITY AND SALE OF OPTIONS

No Option or any right with respect thereto, purchasable hereunder, whether fully paid or not, shall be assignable, transferable or given as collateral or any right with respect to it given to any third party whatsoever, other than by will or by laws of decent and distribution, or as specifically otherwise allowed under the Scheme, except as specifically allowed under the Scheme, and during the lifetime of the Grantee each and all of such Grantee's rights to purchase Shares hereunder shall be exercisable only by the Grantee.

Any such action made directly or indirectly, for an immediate validation or for a future one, shall be void.

12. EFFECTIVE DATE, DURATION, AMENDMENTS OR TERMINATION OF THE SCHEME

12.1 The Scheme shall be effective as of the day it was adopted by the Board and shall teaninate at the end of ten (10) years from such day of adoption (the: "**Termination Date**").

12.2 The Company shall obtain the approval of the Company's shareholders for the adoption of this Scheme and/or the Annexes thereto, or for any amendment to this Scheme and/or the Annexes thereto, if shareholders' approval is required under any applicable law including without limitation the U.S. securities law or the securities laws of other jurisdiction applicable to Options granted to Grantees under this Scheme and/or the Annexes thereto, or if shareholders' approval is required by any authority or by any governmental agencies or national securities exchanges including without limitation the U.S. Securities and Exchange Commission.

12.3 The Board may at any time, subject to the provisions of Section 12.2 above and all applicable law, amend, alter, suspend or terminate the Scheme, provided, however, that

(i) the Board may not extend the term of the Scheme specified in Section 12.1 above and;

(ii) no amendment, alteration, suspension or termination of the Scheme shall impair the rights of any Grantee, unless mutually agreed otherwise by the Grantee and the Company, which agreement must be in writing and signed by the Grantee and the Company.

Earlier termination of the Scheme prior to the Termination Date shall not affect the Board's ability to exercise the powers granted to it hereunder with respect to Options granted under the Scheme prior to the date of such earlier termination.

13. GOVERNMENT REGULATIONS

The Scheme, and the granting and exercise of Options hereunder, and the obligation of the Company to sell and deliver Shares under such Options, shall be subject to all applicable laws, rules, and regulations, whether of the State of Israel or of the United States or any other State having jurisdiction over the Company and the Grantee, including the registration of the Shares under the United States Securities Act of 1933, and the Ordinance and to such approvals by any governmental agencies or national securities exchanges as may be required. Nothing herein shall be deemed to require the Company to register the Shares under the securities laws of any jurisdiction.

14. CONTINUANCE OF EMPLOYMENT OR HIRED SERVICES

Neither the Scheme nor the Grant Notification Letter with the Grantee shall impose any obligation on the Company or an Affiliate thereof, to continue any Grantee in its employ or service, and nothing in the Scheme or in any Option granted pursuant thereto shall confer upon any Grantee any right to continue in the employ or service of the Company or an Affiliate thereof or restrict the right of the Company or an Affiliate thereof to terminate such employment or service at any time.

15. GOVERNING LAW & JURISDICTION

The Scheme shall be governed by and construed and enforced in accordance with the laws of the State of Israel applicable to contracts made and to be performed therein, without giving effect to the principles of conflict of laws. The competent courts of Tel-Aviv, Israel shall have sole jurisdiction in any matters pertaining to the Scheme.

16. TAX CONSEQUENCES

16.1 Any tax consequences to any Grantee arising from the grant or exercise of any Option, from the payment for Shares covered thereby or from any other event or act (of the Company and/or its affiliates, or the Grantee) hereunder shall be borne solely by the Grantee. The Company and/or its affiliates shall withhold taxes according to the requirements under the applicable laws, rules, and regulations, including withholding taxes at source. Furthermore, the Grantee shall agree to indemnify the Company and/or its affiliates and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to the necessity to withhold, or to have withheld, any such tax from any payment made to the Grantee.

16.2 The Company shall not be required to release any Share certificate to a Grantee until all required payments have been fully made.

17. NON-EXCLUSIVITY OF THE SCHEME

The adoption of the Scheme by the Board shall not be construed as amending, modifying or rescinding any previously approved incentive arrangements or as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including, without limitation, the granting of Options otherwise than under the Scheme, and such arrangements may be either applicable generally or only in specific cases.

For the avoidance of doubt, prior grant of options to Grantees of the Company under their employment agreements, and not in the framework of any previous option scheme, shall not be deemed an approved incentive arrangement for the purpose of this Section.

18. MULTIPLE AGREEMENTS

The terms of each Option may differ from other Options granted under the Scheme at the same time, or at any other time. The Board may also grant more than one Option to a given Grantee during the term of the Scheme, either in addition to, or in substitution for, one or more Options previously granted to that Grantee.

19. RULES PARTICULAR TO SPECIFIC COUNTRIES

Notwithstanding anything herein to the contrary, the terms and conditions of the Scheme may be adjusted with respect to a particular country by means of an addendum to the Scheme in the form of an annex (the: "Annex"), and to the extent that the terms and conditions set forth in the Annex conflict with any provisions of the Scheme, the provisions of the Annex shall govern. Terms and conditions set forth in the Annex shall apply only to Options issued to Grantees under the jurisdiction of the specific country that is subject of the Annex and shall not apply to Options issued to any other Grantee. The adoption of any such Annex shall be subject to the approval of the Board and if required the approval of the shareholders of the Company.

*****

CAN-FITE BIOPHARMA LTD.

ANNEX A - ISRAEL
TO THE 2013 GLOBL INCENTIVE OPTION SCHEME

Can-Fite Biopharma Ltd. — Israeli Annex

DEFINITIONS

For purposes of this Annex and the Grant Notification Letter, the following definitions shall apply:

(a) **"Affiliate" -** any "employing company" within the meaning of Section 102(a) of the Ordinance.

(b) **"Approved 102 Option" -** an Option granted pursuant to Section 102(b) of the Ordinance and held in trust by a Trustee for the benefit of the Grantee.

(c) **"Capital Gain Option (CGO)" -** an Approved 102 Option elected and designated by the Company to qualify under the capital gain tax treatment in accordance with the provisions of Section 102(b)(2) of the Ordinance.

(d) **"Controlling Shareholder" -** shall have the meaning ascribed to it in Section 32(9) of the Ordinance.

(e) **"Employee" -** a person who is employed by the Company or its Affiliates, including an individual who is serving as a director or an office holder, but excluding any Controlling Shareholder, all as determined in Section 102 of the Ordinance.

(f) **"ITA" -** the Israeli Tax Authorities.

(g) **"Non-Employee" -** a consultant, adviser, service provider, Controlling Shareholder or any other person who is not an Employee.

(h) **"Ordinary Income Option (010)" -** an Approved 102 Option elected and designated by the Company to qualify under the ordinary income tax treatment in accordance with the provisions of Section 102(b)(1) of the Ordinance.

(i) **"102 Option" -** any Option granted to Employees pursuant to Section 102 of the Ordinance.

(j) **"3(i) Option" -** an Option granted pursuant to Section 3(i) of the Ordinance to any person who is a Non-Employee.

(j) **"Ordinance" -** the Israeli Income Tax Ordinance [New Version] 1961 as now in effect or as hereafter amended.

(k) **"Section 102" -** Section 102 of the Ordinance and any regulations, rules, orders or procedures promulgated thereunder as now in effect or as hereafter amended.

(l) **"Trustee" -** any individual appointed by the Company to serve as a trustee and approved by the ITA, all in accordance with the provisions of Section 102(a) of the Ordinance.

(n) **"Unapproved 102 Option" -** an Option granted pursuant to Section 102(c) of the Ordinance and not held in trust by a Trustee.

For the avoidance of any doubt, it is hereby clarified that any capitalized terms not specifically defined in this Annex shall be construed according to the interpretation given to it in the Scheme.

ANNEX A - ISRAEL

1. GENERAL

1.1 This Annex (the: "**Annex**") shall apply only to Grantees who are residents of the state of Israel at the Date of Grant or those who are deemed to be residents of the state of Israel for the payment of tax at the Date of Grant. The provisions specified hereunder shall form an integral part of the 2013 Global Incentive Option Scheme of Can-Fite Biopharma Ltd. (hereinafter: the "**Scheme**"), which applies to the issuance of options to purchase Shares of Can-Fite Biophauna Ltd. (hereinafter: the "**Company**"). According to the Scheme, options to purchase the Company's Shares may be issued to employees, directors, consultants and service provides of the Company or its affiliates.

1.2 This Annex is effective with respect to Options granted following Amendment no. 132 of the Ordinance, which entered into force on January 1, 2003.

1.3 This Annex is to be read as a continuation of the Scheme and only modifies options granted to Israeli Grantees so that they comply with the requirements set by the Israeli law in general, and in particular with the provisions of Section 102 (as specified herein), as may be amended or replaced from time to time. For the avoidance of doubt, this Annex does not add to or modify the Scheme in respect of any other category of Grantees.

1.4 The Scheme and this Annex are complimentary to each other and shall be deemed as one. In any case of contradiction, whether explicit or implied, between the provisions of this Annex and the Scheme, the provisions set out in the Annex shall prevail.

2. ISSUANCE OF OPTIONS

2.1 The persons eligible for participation in the Scheme as Grantees shall include any Employees and/or Non-Employees of the Company or of any Affiliate; provided, however, that (i) Employees may only be granted 102 Options; and (ii) Non-Employees and/or Controlling Shareholders may only be granted 3(i) Options.

2.2 The Company may designate Options granted to Employees pursuant to Section 102 as Unapproved 102 Options or Approved 102 Options.

2.3 The grant of Approved 102 Options shall be made under this Annex adopted by the Board, and shall be conditioned upon the approval of this Annex by the ITA.

2.4 Approved 102 Options may either be classified as Capital Gain Options ("**CGOs**") or Ordinary Income Options ("**OIOs**").

2.5 No Approved 102 Options may be granted under this Annex to any eligible Employee, unless and until, the Company's election of the type of Approved 102 Options as CGO or OM granted to Employees (the: "**Election**"), is appropriately filed with the ITA. Such Election shall become effective beginning the first date of grant of an Approved 102 Option under this Annex and shall remain in effect at least until the end of the year following the year during which the Company first granted Approved 102 Options. The Election shall obligate the Company to grant *only* the type of Approved 102 Option it has elected, and shall apply to all Grantees who were granted Approved 102 Options during the period indicated herein, all in accordance with the provisions of Section 102(g) of the Ordinance For the avoidance of doubt, such Election shall not prevent the Company from granting Unapproved 102 Options simultaneously.

2.6 All Approved 102 Options must be held in trust by a Trustee, as described in Section 3 below.

2.7 For the avoidance of doubt, the designation of Unapproved 102 Options and Approved 102 Options shall be subject to the terms and conditions set forth in Section 102.

2.8 Implementation of the mechanisms set out in Sections 2.4 and 5.2(ii) of the Scheme shall require the obtaining of a tax ruling from ITA.

3. TRUSTEE

3.1 Approved 102 Options which shall be granted under this Annex and/or any Shares allocated or issued upon exercise of such Approved 102 Options and/or other shares received subsequently following any realization of rights, including without limitation bonus shares, shall be allocated or issued to the Trustee and held for the benefit of the Grantees for such period of time as required by Section 102 or any regulations, rules or orders or procedures promulgated thereunder (the: "**Holding Period**"). In the case the requirements for Approved 102 Options are not met, the Approved 102 Options may be regarded as Unapproved 102 Options, all in accordance with the provisions of Section 102.

3.2 Notwithstanding anything to the contrary, the Trustee shall not release any Shares allocated or issued upon exercise of Approved 102 Options prior to the full payment of the Grantee's tax liabilities arising from Approved 102 Options which were granted to him and/or any Shares allocated or issued upon exercise of such Options.

3.3 With respect to any Approved 102 Option, subject to the provisions of Section 102 and any rules or regulation or orders or procedures promulgated thereunder, a Grantee shall not sell or release from trust any Share received upon the exercise of an Approved 102 Option and/or any share received subsequently following any realization of rights, including without limitation, bonus shares, until the lapse of the Holding Period required under Section 102 of the Ordinance. Notwithstanding the above, if any such sale or release occurs during the Holding Period, the sanctions under Section 102 of the Ordinance and under any rules or regulation or orders or procedures promulgated thereunder shall apply to and shall be borne by such Grantee.

3.4 Upon receipt of Approved 102 Option, the Grantee will sign an undertaking in which he or she will give his or her consent to the grant of the Option under Section 102, and will undertake to comply with the terms of Section 102 and the trust agreement between the Company and the Trustee.

4. THE OPTIONS

The erms and conditions, upon which the Options shall be issued and exercised, shall be as specified in the Grant Notification Letter to be executed pursuant to the Scheme and to this Annex. Each Grant Notification Letter shall state, inter alia, the number of Shares to which the Option relates, the type of Option granted thereunder (whether a CGO, OIO, Unapproved 102 Option or a 3(i) Option), the vesting provisions and the Purchase Price.

5. FAIR MARKET VALUE

Without derogating from the definition of *"Fair Market Value"* enclosed in the Scheme and solely for the purpose of determining the tax liability pursuant to Section 102(b)(3) of the Ordinance, if at the date of grant the Company's shares are listed on any established stock exchange or a national market system or if the Company's shares will be registered for trading within ninety (90) days following the date of grant of the CGOs, the fair market value of the Shares at the date of grant shall be deteimined in accordance with the average value of the Company's shares on the thirty (30) trading days preceding the date of grant or on the thirty (30) trading days following the date of registration for trading, as the case may be.

6. EXERCISE OF OPTIONS

6.1 Options shall be exercised by the Grantee by giving a written notice to the Company and/or to any third party designated by the Company (the: "**Representative**"), in such form and method as may be determined by the Company and, when applicable, by the Trustee, in accordance with the requirements of Section 102, which exercise shall be effective upon receipt of such notice by the Company and/or the Representative and the payment of the Purchase Price for the number of Shares with respect to which the option is being exercised, at the Company's or the Representative's principal office. The notice shall specify the number of Shares with respect to which the option is being exercised.

6.2 Without derogating from Section 4.2 of the Scheme, and in addition thereto, with respect to Approved 102 Options, any shares of Common Stock allocated or issued upon the exercise of an Approved 102 Option, shall be voted in accordance with the provisions of Section 102 and any rules, regulations or orders promulgated thereunder.

7. ASSIGNABILITY AND SALE OF OPTIONS

7.1 Notwithstanding any other provision of the Scheme, no Option or any right with respect thereto, purchasable hereunder, whether fully paid or not, shall be assignable, transferable or given as collateral or any right with respect to them given to any third party whatsoever, and during the lifetime of the Grantee each and all of such Grantee's rights to purchase Shares hereunder shall be exercisable only by the Grantee.

Any such action made directly or indirectly, for an immediate validation or for a future one, shall be void.

7.2 As long as Options or Shares purchased pursuant to thereto are held by the Trustee on behalf of the Grantee, all rights of the Grantee over the shares are personal, can not be transferred, assigned, pledged or mortgaged, other than by will or laws of descent and distribution.

8. INTEGRATION OF SECTION 102 AND TAX ASSESSING OFFICER'S PERMIT

8.1 With regards to Approved 102 Options, the provisions of the Scheme and/or the Annex and/or the Grant Notification Letter shall be subject to the provisions of Section 102 and the Tax Assessing Officer's permit, and the said provisions and permit shall be deemed an integral part of the Scheme and of the Annex and of the Grant Notification Letter.

8.2 Any provision of Section 102 and/or the said permit which is necessary in order to receive and/or to keep any tax benefit pursuant to Section 102, which is not expressly specified in the Scheme or the Annex or the Grant Notification Letter, shall be considered binding upon the Company and the Grantees.

9. DIVIDEND

Subject to the Company's Articles of Association, with respect to all Shares (but excluding, for avoidance of any doubt, any unexercised options) allocated or issued upon the exercise of Options and held by the Grantee or by the Trustee as the case may be, the Grantee shall be entitled to receive dividends in accordance with the quantity of such shares, and subject to any applicable taxation on distribution of dividends, and when applicable subject to the provisions of Section 102 and the rules, regulations or orders promulgated thereunder.

10. TAX CONSEQUENCES

10.1 Any tax consequences arising from the grant or exercise of any Option, from the payment for Shares covered thereby or from any other event or act (of the Company, and/or its Affiliates, and the Trustee or the Grantee), hereunder, shall be borne solely by the Grantee. The Company and/or its Affiliates, and/or the Trustee shall withhold taxes according to the requirements under the applicable laws, rules, and regulations, including withholding taxes at source. Furthermore, the Grantee shall agree to indemnify the Company and/or its Affiliates and/or the Trustee and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to the necessity to withhold, or to have withheld, any such tax from any payment made to the Grantee.

10.2 The Company and/or, when applicable, the Trustee shall not be required to release any share certificate to a Grantee until all required payments have been fully made.

10.3 With respect to Unapproved 102 Option, if the Grantee ceases to be employed by the Company or any Affiliate, the Grantee shall extend to the Company and/or its Affiliate a security or guarantee for the payment of tax due at the time of sale of Shares, all in accordance with the provisions of Section 102 and the rules, regulation or orders promulgated thereunder.

11. GOVERNING LAW & JURISDICTION

This Annex shall be governed by and construed and enforced in accordance with the laws of the State of Israel applicable to contracts made and to be performed therein, without giving effect to the principles of conflict of laws. The competent courts of Tel-Aviv, Israel shall have sole jurisdiction in any matters pertaining to this Annex.

* * *

Attn.: [Grantee's name, I.D. #, address].

Subject: **Israeli Grant Notification Letter**

1. The Company has decided to grant you Options under the Can-fite Biopharma Ltd. 2013 Global Incentive Option Scheme (the: **"Scheme")** and Annex A — Israel to the Scheme (the: **"Israeli Annex"),** duly adopted and approved on November 28, 2013, a copy of which is attached as Exhibit A hereto, forming an integral part hereof Unless otherwise defined herein, capitalized terms used herein shall have the meaning ascribed to them in the Scheme and in the Israeli Annex.

2. The terms of the Option shall commence on the Date of Grant and terminate at the Expiration Date, or at the time at which the Options expire pursuant to the terms of the Scheme and Israeli Annex and as set forth in Exhibit B hereto.

3. The number of Options granted to you as set forth in Exhibit B hereto shall be exercisable for one Share, upon payment of the Purchase Price as set forth in Exhibit B. The Options may be exercised only to purchase whole Shares, and in no case may a fraction of a Share be purchased. If any fractional Share would be deliverable upon exercise, such fraction shall be rounded up one-half or less, or otherwise rounded down, to the nearest whole number.

4. Subject to the provisions of the Scheme, your Options shall vest and become exercisable according to the Vesting Dates as set forth in Exhibit B hereto, provided that you are employed by or providing services to the Company and/or its Affiliates on the applicable Vesting Date.

   For the avoidance of any doubt, you hereby acknowledge that any and all unexercised Options granted to you shall terminate and shall no longer be exercisable on the Expiration Date.

5. You may exercise your Options in accordance with the provisions of Section 7.1 of the Scheme and Section 6 of the Israeli Annex.

6. Notwithstanding anything to the contrary in Section 6.1 of the Scheme and in addition thereto, if in any such Transaction as described in Section 6.1 of the Scheme, the Successor Company (or parent or subsidiary of the Successor Company) does not agree to assume or substitute your Options, the Vesting Dates shall be accelerated so that any of your unvested Option shall be immediately vested in full as of the date which is 7 days prior to the effective date of the Transaction, and the Committee shall notify you that the unexercised Options are fully exercisable for a period of 7 days from the date of such notice, and that any of your unexercised Options shall terminate upon the expiration of such period.

   It is also resolved that if the Successor Company (or parent or subsidiary of the Successor Company) agrees to assume or substitute your Options and your employment with the Successor Company is terminated by the Successor Company without "Cause" within one year of the closing of the Transaction, your Vesting Dates shall be accelerated so that any of your unvested portion of the substituted Option shall be immediately vested in full as of the date of such termination without Cause.

7. You accept and agree that with respect to any Approved 102 Option granted to you, subject to the provisions of Section 102 and any rules or regulation or orders or procedures promulgated thereunder, you shall not sell or release from trust any Share received by you upon the exercise of an Approved 102 Option and/or any share received subsequently following any realization of rights, including without limitation, bonus shares, until the lapse of the Holding Period required under Section 102 of the Ordinance. Notwithstanding the above, you are aware that if any such sale or release occurs during the Holding Period, the sanctions under Section 102 of the Ordinance and under any rules or regulation or orders or procedures promulgated thereunder shall apply to you and shall be borne by you.

   With respect to Approved 102 Options, you hereby acknowledge that you are familiar with the provisions of Section 102 and the regulations and rules promulgated thereunder, including without limitations the type of Option granted to you hereunder and the tax implications applicable to such grant. You accept the provisions of the trust agreement signed between the Company and the Trustee, attached as Exhibit C hereto, and agree to be bound by its terms.

8. Should any Unapproved 102 Option be granted to you, you hereby agree that should you ceases to be employed by the Company or any Affiliate, you shall extend to the Company and/or its Affiliate a security or guarantee for the payment of tax due at the time of sale of Shares, all in accordance with the provisions of Section 102 and the rules, regulation or orders promulgated thereunder.

9. By signing this Grant Notification Letter you are aware and agree that any tax consequences arising from the grant or exercise of any Option, from the payment for Shares covered thereby or from any other event or act (of the Company and/or its Affiliates, the Trustee or yourself), hereunder, shall be borne solely by you. The Company and/or its Affiliates and/or the Trustee shall withhold taxes according to the requirements under the applicable laws, rules, and regulations, including withholding taxes at source. Furthermore, you hereby accept to indemnify the Company and/or its Affiliates and/or the Trustee and hold them harmless against and from any and all liability for any such tax or interest or penalty thereon, including without limitation, liabilities relating to the necessity to withhold, or to have withheld, any such tax from any payment made to you.

   You will not be entitled to receive from the Company and/or the Trustee any Shares allocated or issued upon the exercise of your Options prior to the full payments of your tax liabilities arising from Options which were granted to you and/or Shares issued upon the exercise of Options. For the avoidance of doubt, neither the Company nor the Trustee shall be required to release any share certificate to you until all payments required to be made by you have been fully satisfied.

   Please note that the receipt of the Options and the acquisition of the Shares to be issued upon the exercise of the Options may result in tax consequences. YOU ARE ADVISED TO CONSULT A TAX ADVISER WITH RESPECT TO THE TAX CONSEQUENCES OF RECEIVING OR EXERCISING THIS OPTION OR DISPOSING OF THE SHARES.

10. **Exceptions** By signing this Grant Notification Letter you hereby acknowledge, accept and agree as to the following:

10.1 The Company may in the future issue additional Shares and grant additional Options to various entities and individuals, as the Company in its sole discretion shall determine.

10.2 The Company shall not be obligated to issue any Shares upon the exercise of an Option if such issuance, in the opinion of the Company, might constitute a violation by the Company of any provision of law.

10.3 The transfer of Options and the transfer of Shares to be issued to you upon exercise of the Options shall be subject to the limitations set forth in the Scheme, Israeli Annex and in the Company's Articles of Association and any shareholders' agreement to which the holders of ordinary shares of the Company are bound.

10.4 You shall not dispose any of your Shares in transactions which violate, in the opinion of the Company, any applicable laws, rules and regulations.

10.6 Notwithstanding anything mentioned above and in addition, you are aware that you will have no rights or privileges of a shareholder with respect to any Shares purchasable upon the exercise of an Option, nor shall they be deemed to be a class of shareholders or creditors of the Company for the purpose of all applicable law, until you are registered as a holder of such Shares in the Company's register of shareholders upon exercise of your Options, all in accordance with the provisions of the Scheme.

11. **Miscellaneous** The following shall apply with respect to this Grant Notification Letter and shall be bound by you:

11.1 No Obligation to Exercise Options. The grant and acceptance of the Options granted to you hereunder, imposes no obligation on you to exercise it.

11.2 Confidentiality. You shall regard the information in this Grant Notification Letter and its exhibits attached hereto, as confidential information and you shall not reveal its contents to anyone except when required by law or for the purpose of gaining legal or tax advice.

11.3 Continuation of Employment or Service. Neither the Scheme, the Israeli Annex nor this Grant Notification Letter shall impose any obligation on the Company or any of its Affiliate to continue your employment or service and nothing in the Scheme and/or in the Israeli Annex and/or in this Grant Notification Letter shall confer upon you any right to continue in the employ or service of the Company and/or an Affiliate or restrict the right of the Company or an Affiliate to terminate such employment or service at any time.

11.4 Entire Agreement. Subject to the provisions of the Scheme and/or the Israeli Annex to which this Grant Notification Letter is subject, this Grant Notification Letter, together with the exhibits hereto, constitute the entire agreement between you and the Company with respect to Options granted to you hereunder, and supersedes all prior agreements, understandings and arrangements, oral or written, between you and the Company with respect to the subject matter hereof.

11.5 Failure to Enforce - Not a Waiver. The failure of any party to enforce at any time any provisions of this Grant Notification Letter and/or the Scheme and/or the Israeli Annex shall in no way be construed to be a waiver of such provision or of any other provision hereof.

11.6 Provisions of the Scheme. The Options provided for herein are granted pursuant to the Scheme and the Israeli Annex, and said Options and this Grant Notification Letter are in all respects governed by the Scheme and the Israeli Annex, and subject to all of the terms and provisions of the Scheme and Israeli Annex.

Any interpretation of this Grant Notification Letter will be made in accordance with the Scheme and the Israeli Annex, however, in the event there is any contradiction between the provisions of this Grant Notification Letter and the Scheme and/or the Israeli Annex, the provisions of this Grant Notification Letter will prevail.

By signing this Grant Notification Letter, you hereby represent and warrant that you have accepted the Grant Notification Letter, and have read the Scheme and understand its content and implications including without derogating the restrictions imposed on you under Section 102.

11.7 Binding Effect. The Scheme, the Israeli Annex and this Grant Notification Letter shall be binding upon the heirs, executors, administrators and successors of the parties hereof.

11.8 Notices. All notices or other communications given or made hereunder shall be in writing and shall be delivered or mailed by registered mail or delivered by email or facsimile with written confirmation of receipt to you and/or to the Company at the addresses shown on the letterhead above, or at such other place as the Company may designate by written notice to you. You are responsible for notifying the Company in writing of any change in you address, and the Company shall be deemed to have complied with any obligation to provide you with notice by sending such notice to the address indicated below.

Company's Signature:

By: _____
Can-Fite Biopharma Ltd.

I, the undersigned, hereby acknowledge receipt of a copy of the Scheme and the Israeli Annex and accept the Options subject to all of the terms and provisions thereof. I have reviewed the Scheme, the Israeli Annex and this Grant Notification Letter in its entirety, have had an opportunity to obtain the advice of counsel prior to executing this Grant Notification Letter, and fully understand all provisions of this Grant Notification Letter. I agree to notify the Company upon any change in the residence address indicated above.

[Grantee's full name & Signature]

Exhibit A: **Can-Fite Biopharma Ltd. 2013 Global Incentive Option Scheme & Israeli Annex**

Exhibit B: Terms of the Option's grant

Exhibit C: **Trust Agreement**

EXHIBIT B
TERMS OF THE OPTION

Grantee's name:
Date of Grant:
Designation:

- ☐ Approved 102 Option:
  Capital Gain Option (CGO) ☐;or
  Ordinary Income Option (MO) ☐
- ☐ Unapproved 102 Option
- ☐ 3(i) Option

1. Number of Options granted:
2. Purchase Price:
3. Vesting Dates:

Number of Options	Vesting Date

4. Expiration Date:

Grantee's name

Company

Exhibit 4.34

CERTAIN PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND ARE SUBJECT TO A CONFIDENTIAL TREATMENT REQUEST. COPIES OF THIS EXHIBIT CONTAINING THE OMITTED INFORMATION HAVE BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. THE OMITTED PORTIONS OF THIS DOCUMENT ARE MARKED WITH A […].

CAN-FITE BIOPHARMA LTD

AND

CIPHER PHARMACEUTICALS INC.

DISTRIBUTION AND SUPPLY AGREEMENT

DATED AS OF MARCH 20, 2015

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DISTRIBUTION AND SUPPLY AGREEMENT

between

CAN-FITE BIOPHARMA LTD

and

CIPHER PHARMACEUTICALS INC.

This Distribution and Supply Agreement (the "**Agreement**") is entered into as of March 20, 2015, (the "**Effective Date**") by and between Can-Fite BioPharma Ltd. ("**Can-Fite**"), an Israeli company located at 10 Bareket Street, Kiryat Matalon, PO Box 7537, Petah-Tikva, 49170, Israel, and Cipher Pharmaceuticals Inc. ("**Distributor**"), an Ontario corporation located at 5650 Tomken Road Unit 16, Mississauga Ontario L4W 4P1. Unless otherwise specified, all capitalized terms shall have the meaning specified in Article 1 herein.

RECITALS

1. Can-Fite has the exclusive rights to certain know-how and intellectual property rights relating to the Product;

2. Can-Fite is still in Clinical Development of the Product for the treatment of psoriasis and rheumatoid arthritis and has yet to receive the requisite Approval for the marketing and sale of any therapeutic products which include the Product;

3. Can-Fite wishes, once the Clinical Development is successfully completed and the Approvals are obtained, to have the Product manufactured and packaged for distribution, marketing and sale for use in the Field in the Territory;

4. Distributor has experience in the distribution, marketing and sale of pharmaceutical products in the Territory; and

5. Can-Fite desires to grant Distributor and Distributor desires to accept, the right and obligation to distribute and sell Product for use in the Field in the Territory subject to the terms and conditions of this Agreement.

NOW THEREFORE THIS AGREEMENT WITNESSES THAT in consideration of the foregoing and the covenants and promises contained in this Agreement, the Parties agree as follows:

1. DEFINITIONS

As used herein, the following terms shall have the following meanings:

(a) "**AB Rated Generic**" means a Third Party's product which is deemed by Health Canada to be the therapeutic equivalent of the Product and which contains the same Active Ingredient as the Product.

(b) "**Act**" means the Canada *Food and Drugs Act*, as amended from time to time.

(c) "**Active Ingredient**" means a pharmaceutical compound which is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure or function of the body.

(d) "**Additional Quantity**" has the meaning set forth in Section 6.2(b)(iii).

(e) "**Adverse Drug Experience**" or "**ADE**" means any untoward medical occurrence in a patient administered Product and which does not necessarily have a causal relationship with the Product. An ADE can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of the Product, whether or not considered related to the Product (ICH E2D).

(f) "**Affiliate**" means, with respect to any Party, any other Person directly or indirectly controlling or controlled by, or under direct or indirect common control with, such Party. For purposes of this definition, a Person shall be deemed to "control" any other Person if it owns or controls a sufficient interest in the voting equity (or other comparable ownership if the other Person is not a corporation) such that it can direct, order or control the actions of such other Person and the ownership of fifty percent (50%) or more of the voting equity (or other comparable ownership if the other Person is not a corporation) shall be conclusive evidence of control.

(g) "**Alternate Supplier**" means any Third Party alternate supplier of the Product that Can-Fite used to supply Product for jurisdictions outside the Territory.

(h) "**Approvals**" means collectively the Regulatory Approval and the Other Approvals.

(i) "**Approved Manufacturer**" means Can-Fite and/or a Third Party approved in advance in writing by Distributor (which approval will not be unreasonably withheld or delayed), for the purpose of operating an Approved Manufacturing Site to Manufacture the Supplied Product; provided that all references to Approved Manufacturer(s) shall be intended to include any Alternate Suppliers.

(j) "**Approved Manufacturing Site**" means a manufacturing site at which Supplied Product may be Manufactured, Packaged or Tested in full compliance with the applicable Approvals and all applicable Laws and in the case of an Approved Manufacturer, other than Distributor, or their respective Affiliates, approved in advance in writing by Can-Fite, which approval will not be unreasonably delayed or withheld.

(k) "**Approved Transaction**" has the meaning set forth in Section 8.3.

(l) "**Authorities**" means collectively the Regulatory Authority and the Other Authorities.

(m) "**Authorized Generic**" means the Product marketed as a generic product by Distributor as contemplated by Section 2.4 hereof.

(n) "**Business Day**" means any day other than a Saturday, a Sunday, or a day on which banks in the Province of Ontario, Canada or in Tel-Aviv, Israel are required or authorized to close.

(o) "**Can-Fite Indemnitees**" means any of Can-Fite and Can-Fite's Approved Manufacturers and their respective Affiliates, subsidiaries, equity holders, directors, managers, officers, employees, trustees, representatives, consultants, sublicensees, agents, successors and permitted assigns.

(p) "**Can-Fite Trademarks**" means any trademark, trade name, trade dress, logo, design or associated artwork owned by or licensed to Can-Fite pertaining to the Product, including that listed in Schedule A.

(q) "**Claims**" has the meaning set forth in Section 7.5.

(r) "**Clinical Development**" means clinical studies conducted by Can-Fite or its Affiliates or Sublicensees to seek Regulatory Approval for the Product.

(s) "**COA**" has the meaning set forth in Section 6.5(a).

(t) "**Commercially Reasonable Efforts**" means exercising such reasonable efforts and diligence in accordance with a Party's reasonable business, legal, medical and scientific judgment and in accordance with the efforts and resources a pharmaceutical company similar to the relevant Party would use for a pharmaceutical product which is of similar market potential at a similar stage of its product life, taking into account the competitiveness of the marketplace, the proprietary position of the product and the potential profitability of the product.

(u) "**Competing Product**" means any branded formulations which contain N6-(3-iodobenzyl)-adenosine- 5'-N-methyluronamide ("**IB-MECA**") as an Active Ingredient or any AB Rated Generic.

(v) "**Confidential Information**" means all Intellectual Property and confidential facts relating to the business and affairs of a Party or any of its Affiliates, including financial information, business opportunities, information relating to pharmaceutical products of any nature whatsoever (including Product Information in the case of Can-Fite), know-how (including Product Know-How in the case of Can-Fite), and compilations of information in any form whatsoever; provided, however, that "**Confidential Information**" shall not include any information that (a) was already in the public domain at the time of disclosure, (b) becomes part of the public domain through no action or omission of the receiving Party after disclosure to the receiving party, (c) was already known to the receiving Party, other than under an obligation of confidentiality to the disclosing party, at the time of the disclosure by the other Party, as shown by independent written proof, (d) was independently discovered or developed by the receiving Party without the use of Confidential Information belonging to the disclosing Party as shown by pre-existing written proof, or (e) was disclosed to the receiving Party, other than under an obligation of confidentiality to which a Third Party was subject, by a Third Party who had no obligation to the disclosing Party not to disclose such information to others, as shown by independent written proof.

(w) "**Contract Finisher**" means a Person engaged by any of Can-Fite, an Approved Manufacturer or Distributor to be responsible for Packaging and/or Testing Supplied Product in the Territory.

(x) "Deadline Date" has the meaning set forth in Section 6.2(b)(ii).

(y) "**Dispute**" has the meaning set forth in Section 12.2.

(z) "**Distributor Indemnitees**" means any of Distributor and Distributor's SubDistributors and each of their respective Affiliates, subsidiaries, equity holders, directors, managers, officers, employees, trustees, representatives, consultants, sublicensees, agents, successors and permitted assigns.

(aa) "**Enforcement Action**" has the meaning set forth in Section 7.7(a).

(bb) "**FDA**" means the United States Food and Drug Administration or any successor agency which issues a Regulatory Approval for the Marketing of the Product in the United States.

(cc) "**Field**" means the oral, intravenous and topical use of the Product for treating psoriasis and rheumatoid arthritis in humans and animals.

(dd) "**Firm Order**" has the meaning set forth in Section 6.2(a)(i).

(ee) "**First Commercial Sale**" means the date of the first arm's length sale of a Supplied Product by Distributor, its Affiliates or SubDistributors to a Third Party in the Territory, as evidenced by delivery of the Supplied Product to the Third Party.

(ff) "**Fiscal Year**" means the twelve (12) months ending December 31.

(gg) "**Force Majeure**" means an event or circumstances beyond the reasonable control of a Party or Approved Manufacturer or Contract Finisher and which, with the exercise of diligent efforts that Party or their Approved Manufacturer or Contract Finisher is unable to prevent, including Acts of God, government restrictions, wars, insurrections, failure of suppliers, subcontractors and carriers, strikes, labor disputes, failures of electricity supply and inability to obtain essential ingredients or supplies (for the avoidance of doubt, the Parties agree that the failure of any Approved Manufacturer or a Contract Finisher to supply Can-Fite shall not be deemed a Force Majeure with respect to Can-Fite except to the extent such failure to supply is the direct result of a Force Majeure applicable to such Approved Manufacturer or such Contract Finisher).

(hh) "**Forecast**" has the meaning set forth in Section 6.2(a)(i).

(ii) "**Good Manufacturing Practices (GMP)**" means at any time the quality systems and good manufacturing practices as required by applicable Laws, directives, rules, regulations, guides and guidance in existence in the Territory at that time.

(jj) "**Health Canada**" means Health Canada or any successor agency which issues a Regulatory Approval for the Marketing of the Product in the Territory.

(kk) "**IFRS**" means International Financial Reporting Standards.

(ll) "**Indemnified Party**" has the meaning set forth in Section 10.3.

(mm) "**Indemnifying Party**" has the meaning set forth in Section 10.3.

(nn) "**Initial Milestone Payment**" has the meaning set for in Part A of Schedule C.

(oo) "**Initial Term**" has the meaning set forth in Section 9.1.

(pp) "**Intellectual Property**" means all patents (including the Product Patents in the case of Can-Fite's Intellectual Property), copyrights, trademarks, service marks, service names, trade names, internet domain names, e-mail addresses, applications or registrations for any of the foregoing, or extensions, renewals, continuations or re-issues thereof, or amendments or modifications thereto, brandmarks, brand names, trade dress, labels, logos, know-how (including the Product Know-How in the case of Can-Fite's Intellectual Property), show-how, technical and non-technical information, trade secrets, formulae, techniques, sketches, drawings, models, inventions, designs, specifications, processes, apparatus, equipment, databases, research, experimental work, development, pharmacology and clinical data, software programs and applications, software source documents, Third-Party licenses, and any similar type of proprietary intellectual property right vesting in the owner and/or licensee thereof pursuant to the applicable Laws of any relevant jurisdiction or under any applicable license or contract, whether now existing or hereafter created, together with all modifications, enhancements and improvements thereto.

(qq) "**Joint Steering Committee**" has the meaning set forth in Section 4.9.

(rr) "**Law**" means all laws, statutes, ordinances, decrees, judgments, codes, standards, acts, orders, by-laws, rules, regulations, permits, legally binding policies and guidelines and legally binding requirements of all Regulatory and Other Authorities including the Canada *Food and Drugs Act*, including any amendments thereto, and all regulations, rules, guidelines and procedures promulgated thereunder, as well as analogous legislation in the remainder of the Territory.

(ss) "**Latent Defect**" means a defect that existed at the time that title to Supplied Product passed to Distributor which could not have been detected by Distributor utilizing the Distributor's usual and customary inspection procedures for incoming finished product intended for distribution in the Territory, which in any event will be in accordance with Distributor's GMP obligations.

(tt) "**License Agreement**" means the Patent License Agreement between Can-Fite and the National Institutes of Health designated as L-249-2001/0 together with the First Amendment thereto designated as L-249-2001/1 and the Second Amendment thereto designated as L-249-2001/2.

(uu) "**Losses**" has the meaning set forth in Section 10.1.

(vv) "**Manufacture**" means to make Supplied Product in compliance with GMP, including to process, prepare, make and Test the raw materials used in the preparation of Supplied Product and to Test the Supplied Product prior to release for Packaging, in each case in a finished dosage form ready for administration to humans and "**Manufacturing**" has a corresponding meaning.

(ww) "**Market**" means to promote, advertise, distribute, market, offer to sell and/or sell for purposes of a commercial sale, and "**Marketing**" has a corresponding meaning.

(xx) "**Marketing Plan**" has the meaning set forth in Section 3.2.

(yy) "**Milestone Payments**" means the Milestone Payments, as set forth in Schedule C.

(zz) "**NDS**" or "**New Drug Submission**" means any regulatory submission made by Distributor for Regulatory Approval to Market the Supplied Product, as the same may be amended or supplemented and any related or successor NDS) and shall include all accompanying data and information including supplements and amendments.

(aaa) "**Net Profits**" means with respect to any Authorized Generic authorized to be commercialized by Distributor hereunder [...].

(bbb) "**Net Sales**" means, for any period, the aggregate gross amounts invoiced by Distributor, its Affiliates or SubDistributors in connection with sales of the Product to arm's length Third Parties, (excluding sales of the Distributor to its SubDistributors or Affiliates) for use in the Field in the Territory, less any and all (a) customary discounts or incentives of any type or nature, (such as, without limitation, trade, quantity and cash discounts, charge-backs, recalls, actual returns or rebates or other similar adjustments relating to credits issued to arm's length Third Parties (excluding sales of the Distributor to its SubDistributors or Affiliates)) on such sales, which specifically relate to the Product and are recognized in accordance with Canadian generally accepted accounting principles, (b) customary freight shipping, insurance costs, duties and taxes paid by Distributor or its Affiliates or a SubDistributor on shipment of Product to Distributor, and (c) to the extent not included above, payments under Section 6.7(b). No deductions shall be made for commissions paid to individuals, whether they be with independent sales agencies or regularly employed by Distributor, its Affiliates or SubDistributors, and on its payroll, or for the cost of collections. Notwithstanding the foregoing, in the event Distributor launches an Authorized Generic as contemplated pursuant to Section 2.4 herein, Net Sales for such Authorized Generic shall, in addition to the deductions provided above, allow for discounts and rebates customary in the generic industry that are consistent with Distributor's ordinary course of business in the Territory, provided such discounts and rebates relate solely to the sale of the Authorized Generic.

(ccc) "**Net Selling Price**" means the average selling price per Unit of Product by Distributor, its Affiliates and SubDistributors for use in the Field in the Territory to arm's length Third Party customers (excluding sales of the Distributor to its Affiliates and SubDistributors) of Supplied Product calculated on a monthly basis by dividing the Net Sales of Supplied Product in a calendar month by the number of Units sold in that calendar month in the Territory.

(ddd) "**Official Body**" means any national, federal, provincial or local government or government of any subdivision thereof, or any parliament, legislature, council, agency, authority, board, commission, department, bureau or instrumentality thereof, or any court, tribunal, grand jury, mediator or arbitrator, whether foreign or domestic, in each case having jurisdiction in the relevant circumstances.

(eee) "**Other Approvals**" means, for the Product, the approval or authorization granted by the Other Authorities for the Marketing of the Product for use in the Field in the Territory, including the Pricing Approval and the Reimbursement Approval, as applicable.

(fff) "**Other Authorities**" means Official Bodies (other than the Regulatory Authority) whose approval is required by applicable Law to Market and/or obtain reimbursement for Supplied Product in a jurisdiction in the Territory.

(ggg) "**Package**" means to package and label Supplied Product for Marketing and "Packaging" has a corresponding meaning.

(hhh) "**Parties**" means Can-Fite and Distributor, and "**Party**" means either of Can-Fite or Distributor, as the context requires.

(iii) "**Person**" means any individual, partnership, limited partnership, joint venture, syndicate, sole proprietorship, company or corporation with or without share capital, unincorporated association, trust, trustee, executor, administrator or other legal personal representative or other entity or Official Body.

(jjj) "**Prevailing Party**" has the meaning set forth in Section 12.2.

(kkk) "**Pricing Approval**" means any approval or authorization of any Official Body establishing prices for the Product in a jurisdiction for use in the Field in the Territory.

(lll) "**Product**" means the pharmaceutical preparations described in the Product Patents or associated with the Product Know-How, namely as N6 -(3-iodobenzyl)-adenosine- 5'-N-methyluronamide (IB-MECA) in an oral formulation delivered in bulk or final finished Packaged form for use in humans and meeting the Specifications, as the same may be amended or supplemented, and any related or successor NDSs filed with respect to the same initial application. "Product" also includes any future formulations containing IB-MECA and improvements thereof approved by Health Canada.

(mmm) "**Product Information**" means all in-vivo or clinical, non-clinical, pharmacology, toxicology, safety and efficacy data, stability data, formulary submissions, pharmaco-economic data, and other such information now or hereafter known and available to Distributor or Can-Fite or their respective Affiliates, SubDistributors or Approved Manufacturer(s) or their Affiliates, whether generally known to others or not.

(nnn) "**Product Know-How**" means the data, information, expertise, trade secrets, manufacturing, mixing and production procedures, technical assistance, and shop rights, known to, in the possession of or licensed to Can-Fite, its Affiliates or any Approved Manufacturer(s) or its Affiliates, whether generally known to others or not, and relating to the Manufacturing, Packaging, Marketing and/or Testing of Supplied Product, including:

(i) characteristics, selection of properties and data relating to materials, such as excipients, used or useful in the Manufacturing, Packaging and/or Testing of Supplied Product;

(ii) techniques, equipment and methods used or useful in the Manufacturing, Packaging or Testing of Supplied Product;

(iii) equipment and data relating to the Manufacturing, Packaging or Testing of Supplied Product; and

(iv) all in vivo or clinical, pharmacology, toxicology, safety and efficacy data, formulary submissions, pharmaco-economic data, and other such information useful or required in preparing applications for or obtaining or maintaining Regulatory Approval and/or for the Manufacturing, Packaging, Marketing and/or Testing of Supplied Product.

(ooo) "**Product Liability Claim**" means any Third Party claim involving any actual or alleged death or bodily or emotional injury arising out of or relating to any Supplied Product sold in the Territory for use in the Field.

(ppp) "**Product Patents**" means all patents owned by Can-Fite (i) which have issued as of the Effective Date or (ii) which issue at any time from applications pending as of the Effective Date, or from applications subsequently filed during the Term of this Agreement, which (in the case of both (i) and (ii)) claim, disclose or pertain to inventions necessary or useful for the Manufacture, use, import or Marketing of the Product, including any continuation, division, continuation-in-part, and any provisional applications, and which patents have not expired or been held invalid or unenforceable by a court of competent jurisdiction in a final, non-appealable decision, including all substitutions, extensions, registrations, confirmations, re-examinations, reissues or renewals of such patents. Schedule A lists, as of the Effective Date, all such Patents that have issued and pending applications and Schedule A shall be amended from time to time to include patents or applications owned by or licensed to Can-Fite or one or more of its Affiliates to the extent they claim inventions necessary or useful for Manufacturing, use, import, or Marketing of the Product within the Territory or an amendment to any Product Patents.

(qqq) "**Product Technology**" means collectively Product Know-How and Product Patents.

(rrr) "**Regulatory Approval**" means all approvals or authorizations granted by a Regulatory Authority for the Marketing of Supplied Product for use in the Field in the Territory.

(sss) "**Regulatory Authority**" means Health Canada, and/or any equivalent, similar or successor Official Body, whose approval is required by applicable Law to Market, Manufacture, Test and/or Package Supplied Product in any jurisdiction which forms part of the Territory.

(ttt) "**Regulatory Requirements**" means all applicable Regulatory Approvals, licenses, registrations, GMPs, and authorizations and all other requirements of any applicable Regulatory Authorities in relation to Supplied Product, including each of the foregoing which is necessary for, or otherwise governs, the Manufacture, Marketing, Packaging and Testing of Supplied Product for use in the Field in the Territory.

(uuu) "**Reimbursement Approval**" means any approval or authorization of any Official Body establishing a health insurance or drug reimbursement scheme for Supplied Product in a jurisdiction for use in the Field in the Territory.

(vvv) "**Rejection Notice**" has the meaning set forth in Section 6.5(b).

(www) "**Renewal Term**" has the meaning set forth in Section 9.1.

(xxx) "**Responsible Person**" has the meaning set forth in Section 12.2.

(yyy) "**Resumption Notice**" has the meaning set forth in Section 6.3(b).

(zzz) "**Royalty Percentage**" means 16.5% of Net Sales.

(aaaa) "**Rules**" has the meaning set forth in Section 12.2.

(bbbb) "**Schedules**" means the following Schedules to this Agreement (as the same may be amended from time to time in accordance with this Agreement):

Schedule A - Can-Fite Trademarks and Patents
Schedule B - Specifications
Schedule C - Payments to Can-Fite
Schedule D - Minimum Sales Requirements

(cccc) "**Serious ADEs**" has the meaning set forth in Section 5.1.

(dddd) "**Specifications**" means the specifications of Supplied Product as set forth in Schedule B.

(eeee) "**Stipulated Rejection Period**" has the meaning set forth in Section 6.5(b).

(ffff) "**SubDistributors**" means Third Parties appointed by Distributor pursuant to Section 2.1(c) to Market Supplied Product for use in the Field in the Territory, but shall not include wholesalers, retailers, hospitals, government purchasers or managed and/or care organizations.

(gggg) "**Supplied Product**" means the Product and/or the Authorized Generic, whether or not it is supplied by Can-Fite; provided, however, that any representations, warranties or covenants of Can-Fite herein which refers to Supplied Product only relates to Supplied Product supplied by or on behalf of Can-Fite.

(hhhh) "**Supply Interruption**" has the meaning set forth in Section 6.3(a).

(iiii) "**Tax(es)**" means, with respect to Distributor, all federal, provincial, local, county, foreign and other taxes or government charges constituting sales, use, transfer, value added, customs, duty or excise taxes payable by the Distributor in connection with the importation or sale of Supplied Product.

(jjjj) "**Term**" has the meaning set forth in Section 9.1.

(kkkk) "**Territory**" means Canada.

(llll) "**Test**" means to test a product or its ingredients prior to release for further processing or for shipping and Marketing in compliance with applicable Law and "Testing" has the corresponding meaning.

(mmmm) "**Third Party**" means any Person other than Can-Fite, Distributor or their respective Affiliates.

(nnnn) "**Third Party Laboratory**" means the Third Party Laboratory selected jointly by the Parties for the purpose of adjudicating between them on the matters in disagreement under Sections 5.3(e), 6.6(c) and 6.6(d) below.

(oooo) "**Trademarks**" means any trademark, trade name, trade dress, logo, design or associated artwork selected, owned and/or used by Distributor or its Affiliates pertaining to Supplied Product, other than the Can-Fite Trademarks.

(pppp) "**Transfer Price**" means (i) Can-Fite's cost (as determined in accordance with IFRS) of Manufacturing the Supplied Product, in the event Can-Fite is Manufacturing Supplied Product, or (ii) Can-Fite's actual out-of-pocket cost and expense to procure the Supplied Product from an Approved Manufacturer or Contract Finisher as established from time to time, in the event Can-Fite is procuring Product from an Approved Manufacturer or Contract Finisher, except that if the Approved Manufacturer is an Alternate Supplier, the transfer price shall be no higher than that in effect prior to a Supply Disruption.

(qqqq) "**Unit**" means a single capsule or tablet of Supplied Product.

2. DISTRIBUTION RIGHTS

2.1 Exclusive Distributorship and License.

(a) Upon and subject to the terms and conditions of this Agreement, Can-Fite hereby appoints Distributor as its exclusive distributor of the Product for use in the Field in the Territory throughout the Term with the right and obligation to Market the Product for use in the Field in the Territory and the right to register and develop the Product pursuant to Sections 4.1 and 4.2. Can-Fite represents and warrants to Distributor that, except for the exclusive license granted in this Section 2.1, Can-Fite has not granted any other licenses to use, Market and/or import, the Products for use in the Field in the Territory. The term "exclusive" as used in this Section 2.1(a) means the rights granted to Distributor in this Section 2.1 are to the exclusion of all other persons and entities including Can-Fite. Can-Fite shall take all reasonable and prudent actions to ensure that the Product does not enter the Territory for use in the Field as black market goods.

(b) Distributor shall obtain exclusively from Can-Fite all Supplied Product for Marketing for use in the Field in the Territory, except as otherwise permitted by the terms of this Agreement. Can-Fite shall supply the Supplied Product to Distributor for Marketing by Distributor for use in the Field in the Territory in accordance with the terms of this Agreement and shall not supply the Supplied Product to any other Person for use in the Field in the Territory or to any Person, unless such Person agrees not to knowingly directly or indirectly through Third Parties sell the Supplied Product for use in the Field in the Territory.

(c) Distributor shall have the right to appoint SubDistributors to Market the Supplied Product for use in the Field solely within the Territory, and Distributor shall cause such SubDistributors to perform the applicable obligations of Distributor under this Agreement, or otherwise ensure that such obligations are performed by the Distributor. Distributor shall remain fully responsible and liable to Can-Fite for the performance of all of the terms of this Agreement by its SubDistributors. Distributor shall not be entitled to appoint as a SubDistributor any Person which is or has engaged in, directly or indirectly, developing or Marketing any Competing Product in the Territory.

(d) Can-Fite hereby grants to Distributor an exclusive license (including the right to grant sublicenses to SubDistributors) for use in the Field in the Territory to (i) all Product Technology necessary or useful in order to Market the Supplied Product, (ii) clinical, non-clinical and safety data in order to obtain Regulatory Approval, and Pricing Approval or Other Approvals in the Territory, and (iii) a Canadian URL for the Product.

(e) Except as expressly provided in this Agreement, Can-Fite is not granting to Distributor any right, title or interest, whether express or implied, in the Product or any Intellectual Property or other right that Can-Fite or its Affiliates may own or control.

(f) Notwithstanding anything contained herein, Can-Fite is not granting to Distributor any rights under the License Agreement.

2.2 Restrictions on Marketing of Products.

From and after the Effective Date, Distributor shall not, and shall cause its Affiliates and SubDistributors to not, Market or export the Supplied Product outside the Territory or outside the Field, or Market or export the Supplied Product to any Person who, to the knowledge of any of Distributor, its SubDistributors, or its Affiliates, intends to directly or indirectly Market or export Product outside the Territory or outside the Field.

2.3 Covenant Not to Market Competing Products.

From and after the Effective Date until the earlier of termination of this Agreement or the launch of an AB Rated Generic by a Third Party within the Territory, Distributor shall not, and shall cause its Affiliates and SubDistributors to not Market a Competing Product in the Territory.

Can-Fite agrees that during the Term neither it nor its Affiliates will Market and/or import, the Product or any Competing Product for use in the Field in the Territory, nor license or otherwise authorize any Third Party to develop, Market, Manufacture for sale inside the Territory for use in the Field, and/or import the Product or any Competing Product for use in the Field in the Territory.

2.4 Authorized Generics.

In the event that a Third Party launches an AB Rated Generic in the Territory, Distributor may sell an Authorized Generic for use in the Field in the Territory, provided that Distributor pays Can-Fite [...] of Net Profits in the Territory and no other payments other than Transfer Price payments (to the extent Can-Fite is supplying the Authorized Generic) will be due to Can-Fite with respect to such sales.

3. MARKETING

3.1 Marketing Decisions.

Distributor shall control and make all decisions regarding the strategy and tactics of Marketing, selling and otherwise commercializing the Products for use in the Field in the Territory, including, without limitation, the methods of sale and distribution, organization and management of sales and Marketing, Packaging, pricing, and Labeling, appointment of SubDistributors, and other terms and conditions of such sales and Marketing. Notwithstanding the aforesaid, Distributor shall consult with Can-Fite prior to taking any material decision regarding the strategy and tactics of Marketing, selling and otherwise commercializing the Products in the Territory.

3.2 Marketing Plan.

Distributor will be responsible for assessing the market opportunities for the Product for use in the Field in the Territory and preparing and providing to Can-Fite, at least six (6) months prior to the First Commercial Sale, a marketing plan for the Product ("**Marketing Plan**") which Marketing Plan shall set forth Distributor's plan, strategy and proposed activities consistent with efforts appropriate for pharmaceuticals products of similar market potential to market the Product in the Territory. The Marketing Plan will include as appropriate without limitation, the following elements,

(a) a description of Distributor's general strategy with respect to pre-launch and post-launch marketing, reimbursement strategies, advertising and promotion activities of the Product in the Territory;

(b) an estimated time schedule for the performance of the marketing activities;

(c) a description of the personnel resources of Distributor that will perform the marketing activities, including the number of sales representatives and physician calls; and

(d) a description of Distributor's pricing strategy in the Territory.

Thereafter, Distributor shall, on or before November 1st in each Fiscal Year of the Term provide Can-Fite with a copy of Distributor's Marketing Plan for the next Fiscal Year. Can-Fite may communicate comments to Distributor in respect of such Marketing Plans. Distributor agrees to consider such comments and shall provide a response to Can-Fite in respect of such comments, which response may include revisions to the Marketing Plan. Notwithstanding the foregoing, Distributor shall determine the Marketing Plan and will be responsible for its implementation and shall use Commercially Reasonable Efforts to achieve the objectives specified therein.

3.3 Advertising and Promotion.

Distributor shall provide to Can-Fite copies of the materials relating to the Marketing of the Supplied Products including print advertising and similar materials on a timely basis. All such materials shall comply in all material respects with applicable Laws and requirements of any applicable Regulatory Authority. Distributor shall not, in its Marketing materials, make any therapeutic claims or statements relating to the Supplied Products other than those authorized by the applicable Regulatory Authorities, and Distributor shall remain solely liable for all Marketing materials relating to the Supplied Products.

3.4 Information Sharing.

Can-Fite shall provide to Distributor in English such Product Information known to Can-Fite that may be useful or that Distributor requests or requires in preparing applications for or obtaining any Other Approvals and/or in the Marketing of the Product within the Territory, or in obtaining formulary listings or acceptance or approval of the Product by customers, potential customers, or buying agents or groups within the Territory. Distributor shall, and shall require its Affiliates and SubDistributors to, promptly provide to Can-Fite all Product Information that comes into its possession and all information relating to the Marketing or use of the Product.

3.5 Reports.

(a) Each Party shall promptly keep the other fully informed of all governmental and regulatory requirements, activities and plans of any Regulatory Authority including any changes thereto of which such Party becomes aware which materially affect, or are reasonably likely to materially affect, the sales or distribution of the Product in the Territory.

(b) After the First Commercial Sale of the Product, Distributor shall, throughout the Term, provide to Can-Fite on a calendar quarterly basis a statement containing the number of Units sold, the gross sales, the Net Sales and the Net Selling Price for each Product including details of all necessary calculations of the same, including the calculations which detail the differences between Net Sales and gross sales during such calendar quarter. Distributor shall provide such statement on a quarterly basis on or before the forty-fifth (45th) day following such calendar quarter.

(c) After the First Commercial Sale of the Product, Distributor shall on a calendar basis provide on or before the thirtieth (30^{th}) day following each Fiscal Year, a report summarizing the status of Other Approvals and filings in terms of formulary listings and reimbursement pricing tier for each listing if applicable.

4. REGULATORY MATTERS AND PRODUCT DEVELOPMENT

4.1 Registration Responsibilities.

Distributor, provided that Can-Fite has, and continues to, comply with its covenants and obligations set forth in this Agreement, shall conduct and be responsible for:

(a) preparing the NDS or other applications, filing drug approval applications, including the NDS, answering any filing review issues and meeting with Regulatory Authorities;

(b) obtaining from the relevant Regulatory Authorities in the Territory, and for maintaining in force, all Regulatory Approvals in the Territory in Distributor's name;

(c) the work for submitting variations to the Regulatory Approvals, the renewal of the Regulatory Approvals or any other regulatory procedure, answering any filing review issues and meeting with Regulatory Authorities; and

(d) paying all costs and expenses in connection with the costs of obtaining Regulatory Approval within the Territory.

Can-Fite acknowledges that Distributor, notwithstanding its efforts, does not guarantee that its efforts will result in the approval by Health Canada of the NDS or the issuance of any or all required Regulatory Approvals.

Can-Fite, upon written request of Distributor, shall provide Distributor, in English, with the Product Information and any requested or necessary documents relating to the Products (sufficient quantity of standard and working samples) and/or other information, for carrying out registration of the Products, making the NDS filing, and procuring the Regulatory Approvals in the Territory.

4.2 Development Responsibilities.

Can-Fite shall be responsible for all Product development activities including management of the clinical studies required in order to secure Regulatory Approval and shall use Commercially Reasonable Efforts in conducting such activities. Can-Fite agrees to include Canadian clinical sites in the pivotal phase III (or phase II/III, as applicable) Clinical Development program. Distributor shall not be responsible for any research and development costs associated with the Product. Distributor acknowledges that Can-Fite, notwithstanding its efforts, does not guarantee that its efforts will result in the success of any Clinical Development or that the Product will be found to be effective and be able to be Marketed and sold in the Territory for use in the Field.

4.3 Post-Approval Regulatory Responsibilities.

(a) Distributor shall be responsible for all pharmacovigilance activities related to the Supplied Product for use in the Field in the Territory.

(b) All substantive and material communications by Distributor with the Regulatory Authority for use in the Territory relating to the Supplied Product as Marketed for use in the Field in the Territory shall be promptly provided in writing to Can-Fite, and Distributor shall promptly provide to Can-Fite copies of all documents sent to or received from the Regulatory Authority regarding the Supplied Product.

(c) Distributor shall have the right, at its sole cost and expense, to conduct any post-regulatory approval, clinical Testing that Distributor chooses to conduct with respect to the Supplied Product that has received Regulatory Approval for use in the Field in the Territory, if any, for the continued and successful Marketing of the Supplied Product for use in the Field in the Territory. Notwithstanding the aforesaid, Distributor shall consult with Can-Fite prior to taking any material decision regarding the conduct of any such post regulatory approval or clinical Testing.

4.4 Other Approvals.

Distributor shall be responsible for all matters relating to the Other Approvals for the Product including filing the Product with, maintaining the Product on and dealing with, any federal, provincial or private formularies. The Distributor will apply for and will hold the Other Approvals in the Distributor's name at all times for the benefit of Can-Fite. Distributor shall be responsible for all regulatory filings relating to the Product with the Other Authorities.

4.5 Monitoring ADE and Quality Complaint.

Distributor shall be responsible for receiving, monitoring, responding promptly to, tracking, or as may otherwise be required by applicable Law and Regulatory Authority, all Product-related inquiries, Product quality complaints, and ADE reports received by Distributor, its Affiliates or SubDistributors or by Can-Fite (and which Can-Fite shall have forwarded to Distributor) from individuals and/or health care professionals from within the Territory regarding the Supplied Product.

4.6 Quality and Technical Agreement.

The Parties shall negotiate in good faith and enter into a quality and technical agreement that appropriately addresses each Party's responsibilities as they relate to Manufacturing, storage, distribution, regulatory, operational, Testing and quality issues regarding the Supplied Product no later than six (6) months prior to the First Commercial Sale (as such quality and technical agreement may be amended from time to time during the Term by mutual agreement of the Parties or to conform to requirements of applicable Law).

4.7 Pharmacovigilance Agreement.

The Parties shall negotiate in good faith and enter into a pharmacovigilance agreement that appropriately addresses each Party's responsibilities as they relate to pharmacovigilance no later than six (6) months prior to the First Commercial Sale (as such pharmacovigilance agreement may be amended from time to time during the Term by mutual agreement of the Parties or to conform to requirements of applicable Law).

4.8 Cooperation.

Each of Can-Fite and Distributor shall provide to the other or if applicable, directly to the Authorities, any assistance and all documents reasonably necessary to enable the other to carry out its obligations under this Article 4. In general, requests for cooperation should be responded to by the other party within three (3) Business Days and both should make responsible efforts to ensure cooperation is maintained to ensure completion of the given project.

4.9 Joint Steering Committee.

A joint steering committee ("**Joint Steering Committee**") will be established to monitor and supervise the progress of clinical studies and any other studies relating to development of the Product. The Joint Steering Committee will be composed of members as determined by Can-Fite, provided that the Joint Steering Committee includes one member from Distributor. A member determined by Can-Fite shall chair the Joint Steering Committee and in such capacity shall set its agenda and shall document the discussions held. The Joint Steering Committee will meet (in person or telephonically) as often as is reasonably necessary to accomplish its purpose but at least quarterly, on a mutually agreeable date and at a mutually agreed place. The Joint Steering Committee will make recommendations but will have no formal decision making authority as to the clinical studies. The Joint Steering Committee will dissolve once all Regulatory Approvals have been received for the Product.

5. ADES, PRODUCT QUALITY AND PRODUCT RECALLS

5.1 ADEs.

Each of Can-Fite and Distributor and their respective Affiliates, SubDistributors, Approved Manufacturers, agents or other relevant parties shall inform the other of all known or suspected ADE's associated with Supplied Product, of which it is notified, or otherwise becomes aware, as soon as reasonably possible but in any event within ten (10) days for ADEs and forty-eight (48) hours for Serious ADEs or within any time limits required by applicable Law, whichever is shorter. "**Serious ADEs**" means, with respect to a serious adverse event or reaction, is any noxious and unintended response to a drug that at any dose:

- requires in-patient hospitalization or prolongation of existing hospitalization;

- causes congenital malformation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly/birth defect;
- is a medically important event or reaction;
- results in death; or
- is life-threatening.

5.2 Product Complaints other than ADEs.

(a) Each Party shall submit to the other Party, within three (3) Business Days of receipt any complaints or issues that question Supplied Product quality (other than ADEs or performance of the Supplied Product) received by that Party or any of its Affiliates or, in the case of Distributor, its SubDistributors, to which that Party must respond, together with all evidence then available and all other information relating thereto subsequently obtained or produced by either Party.

(b) Can-Fite shall respond, in writing (including by email) or by telephone, to inquiries made by Distributor relating to the Manufacturing or Packaging of Supplied Product as promptly as practicable, but in no event, later than fifteen (15) Business Days of receipt of the such inquiry, with such information as Distributor may reasonably require addressing the inquiry.

(c) Each of Distributor and Can-Fite shall promptly notify the other of any notice of non-compliance with any Laws applicable to Supplied Product or the Packaging of Supplied Product, received from any Authority having jurisdiction in the Territory, and of any request for or initiation of any inspection of any facility of either Can-Fite or Distributor, or any Affiliate of Can-Fite or Distributor, or any Approved Manufacturer, or Contract Finisher that Manufactures, Packages, Tests or stores any Supplied Product.

(d) Each Party shall inform the other of all known or suspected adverse drug reactions associated with the Product (not otherwise covered above), of which it is notified, or otherwise becomes aware, within two (2) weeks, together with all evidence then available and all other information relating thereto subsequently obtained or produced by either Party.

5.3 Product Recall.

(a) Distributor will maintain or cause to be maintained such traceability records as are necessary to permit a recall, market withdrawal or field correction of the Supplied Product including inventory withdrawal in connection with any of the foregoing (each a "**Recall**").

(b) Each Party shall promptly (but in any case, not later than twenty-four (24) hours of receipt) notify the other Party in writing of any information which indicates a Recall of any Supplied Product may be necessary, any safety or regulatory concerns, or any order, request or directive of a court or other Regulatory Authority requesting or requiring a Recall.

(c) To the extent permitted by circumstances, the Parties will confer before initiating any Recall. If the Parties do not agree on the need for or the extent of such a Recall, either Party may authorize the Recall.

(d) Distributor shall be responsible for the carrying out of any and all Recalls with respect to the Supplied Product in accordance with applicable Laws.

(e) If any Recall is required primarily and substantially because of (i) breach of Can-Fite of a representation, warranty or covenant hereunder, or (ii) failure of the Supplied Product to conform to the Specifications at the time title is transferred to the Distributor, as confirmed by a mutually acceptable Third Party Laboratory, including a Latent Defect that is shown to have existed at the time of such title transfer, Can-Fite will be responsible for the direct costs of such Recall, will reimburse Distributor, its Affiliates, and SubDistributors for all of their direct out-of-pocket costs and direct expenses related to such Recall. The Parties shall promptly discuss whether to credit or refund the Transfer Price of any Supplied Product subject to any Recall and, if the Parties are unable to agree, then Can-Fite shall supply to Distributor free of cost and expense replacement Supplied Product and Distributor will distribute the replacement Supplied Product.

(f) If any Recall is required primarily or substantially in circumstances caused by the negligence, mistake, fault, error or omission of Distributor, its Affiliates or subcontractors, including any breach by Distributor of a representation, warranty or covenant hereunder, Distributor will be responsible for the direct costs of such Recall and will reimburse Can-Fite and its Affiliates for all of their direct out-of-pocket costs and direct expenses related to such Recall.

(g) If any Recall is required under circumstances not covered in Clauses (e) or (f) above, the parties will equally share the direct costs of such Recall, including direct out-of-pocket costs and expenses related to such Recall.

5.4 Cooperation as to ADE, Product Inquiries and Recalls.

Each of Can-Fite and Distributor shall provide to each other in a timely manner all information which the other Party reasonably requests regarding Supplied Product in order to enable the other Party to comply with all Laws applicable to Supplied Product in the Territory and in order to enable Can-Fite to comply with all Laws applicable to the Product outside the Territory. Without limiting the foregoing, each Party will cooperate fully with the other Party in connection with any Recall efforts.

6. PURCHASE PRICE AND SUPPLY OF PRODUCTS

6.1 Supply of Products.

(a) Can-Fite will be responsible for the Manufacture of Supplied Product and shall cause its Approved Manufacturer to Manufacture and, if applicable, its Contract Finisher to Package and label the Supplied Product for the Distributor. Except as provided in Section 6.3, the Distributor shall purchase from Can-Fite all of the Distributor's requirements for the Supplied Product for use in the Field in the Territory during the Term, pursuant to purchase orders submitted by the Distributor or its Affiliates to Can-Fite from time to time in accordance with Section 6.2.

(b) Except as provided in Section 6.3, Can-Fite shall supply or cause the Approved Manufacturer to supply all Supplied Product for use in the Field for distribution in the Territory solely to Distributor during the Term in accordance with the terms and conditions of this Agreement.

(c) Can-Fite and its Approved Manufacturer and if applicable its Contract Packager shall be responsible for the purchase of adequate supplies of all materials, including, without limitation, raw materials, in accordance with the NDS and other filings with Regulatory Authorities for the Supplied Product as necessary to supply finished Supplied Product to the Distributor in accordance with the Specifications and applicable Law.

(d) The Supplied Product shall be manufactured with labeling and packaging as specified by Distributor and in accordance with applicable Laws. At least four (4) months prior to the First Commercial Sale with respect of each Supplied Product, Distributor shall, at its sole cost and expense, provide Can-Fite with final specifications for such labeling and packaging for Supplied Product, including all necessary photo-ready artwork (or its substantial equivalent). Distributor, from time to time may update the labeling and packaging specifications. Such updates shall be subject to the prior written approval of Can-Fite, not to be unreasonably withheld, delayed or conditioned. Distributor shall, at Distributor's expense, use Commercially Reasonable Efforts to secure any approvals required by Health Canada or any other applicable Regulatory Authority to effect such revisions to the labeling and packaging.

(e) The terms and conditions of this Agreement shall control the Manufacture and supply of Supplied Product by Can-Fite to Distributor, and no terms or conditions contained in any purchase order, acknowledgment, invoice, bill of lading, acceptance or other pre-printed form issued by any Party shall have any force or effect to the extent they are inconsistent with or modify the terms and conditions of this Agreement including those set forth in this Section 6.1.

(f) Out-of-pocket costs associated with regulatory changes requested by (i) Health Canada which cause finished product, raw materials, labeling and other materials to be discarded will be shared equally between Distributor and Can-Fite, and (ii) Distributor which cause finished product, raw materials, labeling and other materials to be discarded will be borne by Distributor.

(g) The costs of implementing, chemistry, manufacturing and controls changes or ancillary additional testing not included in the New Drug Submission that is requested after Regulatory Approval, validation and launch, shall be shared equally between Distributor and Can-Fite if requested by a Regulatory Authority and shall be borne one hundred percent (100%) by Distributor, if requested by Distributor.

6.2 Forecasts, Orders.

(a) Forecasts; Firm Orders.

(i) Distributor shall submit to Can-Fite, at least four (4) months prior to the estimated First Commercial Sale, a written forecast for the first twelve (12) month period of the quantity of Supplied Product (a **"Forecast"**) that Distributor desires to have delivered to it for Product launch purposes. The Parties agree that the Supplied Product quantities specified in Distributor's initial Firm Order, represent Distributor's launch quantities of the Supplied Product. Thereafter, on or before the tenth (10) calendar day of each month during the Term, Distributor shall provide a written, updated consecutive twelve (12) month Forecast (on 10th of January, the Forecast will be until the 10th of January of the next year, on 10 of February, the Forecast will be until the 10 of February of the next year, etc) of the Supplied Product, including the expected purchase order dates and shipping dates for each order during the following twelve (12) consecutive calendar month period beginning on the first day of the following calendar month. Can-Fite acknowledges that such Forecasts are only estimates of Distributor's purchase order requirements of the Supplied Product and that Distributor shall not be bound by any such estimate, except that beginning after the First Commercial Sale (A) the portion of the Forecast commencing on the first day of the Forecast period and ending on the last day of the third full calendar month after the first day of the Forecast period shall be deemed a firm order period for which Distributor is obligated to issue purchase orders and take ownership of Supplied Product requirements (each, a "**Firm Order**") and (B) the first two months of each Forecast will repeat the balance of the Firm Order period of the prior Forecast, and the first three months of the Forecast shall constitute the new Firm Order period for which Distributor is obligated to purchase and take delivery of the forecasted Supplied Product, and (C) the third month of the Firm Order period may vary by up to twenty percent (20%) from that set forth on the fourth month of the prior Forecast.

(ii) Can-Fite shall have no liability to Distributor for any failure or inability to supply Distributor in the third month of the Firm Order, with quantities of Product in excess of amounts described in Section 6.2(a)(i)(C).

(iii) Can-Fite shall notify Distributor if Can-Fite determines that it will be unable to meet the quantities of Supplied Product in excess of Can-Fite's obligations as contemplated in Section 6.2(a)(ii), as soon as practicable but in any event within ten (10) days after receiving the applicable purchase orders from Distributor.

(b) Purchase Orders.

(i) Distributor shall deliver to Can-Fite its initial purchase order for the Product within one hundred and twenty (120) days prior to the shipping date required by Distributor. The initial purchase order for the Product shall be for sufficient quantities to satisfy sales requirements of Distributor for no less than the first three (3) months of sales of Product. The purchase order shall specify the location to which Product is to be shipped (which is not the same as where title passes under Section 6.4) and the date by which Product must be shipped to such location.

(ii) During the Term, Distributor shall submit to Can-Fite, purchase orders for the last month of each Firm Order period no later than one hundred and five (105) days (**"Deadline Date"**) prior to the required shipping date, identifying the quantities of Supplied Product. The purchase order shall also specify the location to which Product is to be shipped (which is not the same as where title passes under Section 6.4) and the date by which the Product must be shipped to such location. Such purchase orders shall comply with the Firm Order period provisions set out in Section 6.2(a). If a purchase order for any month is not submitted by the Deadline Date, Distributor shall be deemed to have submitted a purchase order for such month for the amount of Supplied Product set forth in Distributor's most recent Forecast for such month.

(iii) In the event that a purchase order requires an amount higher than one hundred and twenty percent (120%) of the amount set forth in the Forecast for a given month (the "**Additional Quantity**"), Can-Fite shall either (i) confirm to Distributor its acceptance of such purchase order with respect to the Additional Quantity within ten (10) calendar days of receipt of such purchase order or (ii) in the event that Can-Fite cannot supply the Additional Quantity indicated in such purchase order, Can-Fite shall provide Distributor within such ten (10) day period with a delivery schedule for such Additional Quantity which Can-Fite will commit to meet.

(c) Batch Sizes. Once the validation batch inventories have been depleted, Forecasts and purchase orders shall be in minimum batch sizes which are commercially reasonably under the specific circumstances of this Agreement as determined by the parties jointly in good faith.

(d) Satisfaction by Can-Fite Affiliates and Approved Manufacturers. Can-Fite may cause any Affiliate or its Approved Manufacturer to satisfy any of the obligations of Can-Fite under this Article 6. Notwithstanding the previous sentence, Can-Fite shall remain fully responsible and liable to Distributor for the performance of all terms of this Article 6 by its Affiliates or Approved Manufacturers.

(e) Alternative Delivery of Forecasts and Payments. Can-Fite may direct Distributor, in writing, to deliver its Forecasts, purchase orders and payments to an Affiliate of Can-Fite or an Approved Manufacturer, with a copy to Can-Fite, and to receive shipments of a Supplied Product from that Affiliate or Approved Manufacturer.

(f) Form of Purchase Orders. All purchase orders placed by Distributor hereunder shall be in a form reasonably acceptable to Can-Fite, and Distributor shall send such purchase orders by email, courier or mutually agreed upon method. Except for terms relating only to quantities, shipping dates and delivery destinations, none of the terms and conditions contained in any purchase order, invoice or similar documents shall have any effect upon or change the provisions of this Agreement unless signed by both Parties and specifically stating that the Parties intend to vary the terms hereof.

6.3 Continuity of Supply.

(a) A "**Supply Interruption**" shall have occurred in the event that (i) Can-Fite is unable to supply any Supplied Product to Distributor pursuant to Section 6.2 for sixty (60) days or more of the anticipated date of delivery specified in a purchase order, to the location specified therein, or (ii) Can-Fite is unable to deliver on a timely basis at least eighty-five percent (85%) of the amount covered by Purchase Orders issued by Distributor pursuant to Sections 6.2(b) for four (4) or more consecutive months, (whether as a result of a Force Majeure event, GMP issues, failure to meet quality standards, or otherwise). In the event that circumstances arise that may give rise to a potential Supply Interruption, the Parties will work collaboratively in good faith to avoid a Supply Interruption and in such case Can-Fite agrees to use Commercially Reasonable Efforts to provide Distributor with the same or greater percentage of Supplied Product for its Firm Orders, as the percentage of Supplied Product it provides to any other distributor of Product outside the Territory with respect to its Firm Orders; provided, however, that the foregoing shall not lessen or adversely impact Distributor's rights under this Section 6.3. Without limiting the foregoing, Can-Fite's Commercially Reasonable Efforts shall include without limitation sourcing Product from Alternate Suppliers, and Can-Fite shall supply or shall cause such Alternate Supplier to sell Product to Distributor, on the same terms and conditions as Distributor was otherwise purchasing Supplied Product from Can-Fite hereunder, provided that Distributor shall approve, such approval not to be unreasonably withheld, any Alternate Supplier prior to purchasing any Product manufactured by such Alternate Supplier.

(b) Can-Fite shall have six (6) months from the date of the occurrence of the Supply Interruption to resume compliance with its supply obligations in accordance with this Agreement. Can-Fite shall provide Distributor with written notice of its ability to resume supply (the "**Resumption Notice**"), if Can-Fite is able to resume supply within such six (6) month period. The Resumption Notice must: (i) list the date on which Can-Fite will be able to resume its supply obligations (which must not be later than one month from the date of the notice; and (ii) include a statement of Can-Fite's ability to resume such obligations by that date which describes in reasonable detail what problems have been rectified and include a representation (which will be deemed a Can-Fite representation under this Agreement) that Can-Fite is able to fulfill its supply obligations under this Agreement.

(c) If a Supply Interruption occurs and Can-Fite is not able to resume supply within the six (6) month period provided in Section 6.3(b), then Distributor will have the right, but not the obligation, in its sole discretion upon written notice to Can-Fite, to terminate this Agreement.

6.4 Method of Delivery of Supplied Product.

Can-Fite shall notify Distributor of, as applicable, the location of the Approved Manufacturer or Contract Finisher and of any change thereto. Distributor shall advise Can-Fite in writing at least fifteen (15) days in advance of the scheduled shipping date specified in the applicable purchase order of the carrier to be used to ship Supplied Product to Distributor. Distributor will cause such carrier to comply with all applicable Laws for the shipment of Supplied Product. Can-Fite shall determine the appropriate carrier if Can-Fite receives no direction from Distributor at least fifteen (15) days in advance of the scheduled shipping date specified in the applicable purchase order to use a particular carrier. Can-Fite shall deliver all quantities of Supplied Product to Distributor FCA (Incoterms 2010) the manufacturing facility or warehouse of Distributor, its Approved Manufacturer or Contract Finisher and risk of loss and title to Supplied Product shall pass to Distributor immediately upon the loading of Supplied Product at such facility or warehouse. Distributor shall be responsible for all freight, insurance, handling, fees, taxes and other costs associated with shipment or importation of Supplied Product.

6.5 Acceptance, Rejection and Revocation of Acceptance.

(a) Can-Fite shall provide a certificate of analysis and other documents (collectively, the "**COA**") in such forms as the Parties shall mutually agree upon, for any Supplied Product batch delivered to Distributor hereunder certifying that such Supplied Products have been Manufactured and Packaged in compliance with the Specifications, GMPs and all other applicable Regulatory Requirements and with an expiry date of not less than thirty (30) months from the date of shipment.

(b) Distributor shall inspect or shall cause to be inspected all shipments of Supplied Product promptly upon receipt. Distributor may reject any Supplied Product which does not conform to the Specifications at the time of receipt at Distributor's location. Distributor shall make any such rejection in writing, within thirty (30) days of the later of the receipt of the COA or the Supplied Product at the facility designated by Distributor in the applicable Purchase Order (the "**Stipulated Rejection Period**"), to Can-Fite, and shall indicate the reasons for such rejection (the "**Rejection Notice**").

(c) If Distributor has not delivered a Rejection Notice within the Stipulated Rejection Period, Distributor shall be deemed to have accepted that shipment of Supplied Product. Once Distributor has accepted or has been deemed to have accepted a shipment of Supplied Product, and except with respect to Latent Defects discovered by Distributor or Distributor's customers after the expiration of the Stipulated Rejection Period, Distributor may not exercise any rights to subsequently reject such shipment under this Section 6.5.

6.6 Rejection Procedures.

(a) After Can-Fite receives the Rejection Notice, it will evaluate process issues and the reasons given by Distributor for the Rejection. Can-Fite shall use good faith efforts to promptly notify Distributor whether it agrees with the basis for Distributor's rejection, but in no event shall such notice be given later than thirty (30) days of Can-Fite's receipt of a Rejection Notice. If Can-Fite does not so notify Distributor within thirty (30) days of receipt of the Rejection Notice as to whether it agrees with the basis of Distributor's rejection, Can-Fite shall be deemed to be in agreement therewith.

(b) If Can-Fite agrees with or is deemed to agree with the basis for Distributor's rejection, Can-Fite shall promptly replace, at no cost to the Distributor, such rejected Supplied Product.

(c) If Can-Fite disagrees with the basis for Distributor's rejection specified in the Rejection Notice, Can-Fite shall promptly replace such rejected Supplied Product. No payment shall be due with respect to the replacement Product until it is determined which Party shall bear the burden of such cost hereunder. The Parties shall submit samples of the rejected Supplied Product to the Third Party Laboratory, which shall determine whether such Supplied Product meets the Specifications and, as part of this process, may also carry out a full investigation of the Manufacturing process (including, as necessary, the Approved Manufacturing Site) for such Supplied Product if it reasonably believes such an investigation is necessary to resolve the disagreement. The Parties agree that the determination of the Third Party Laboratory, after it has assessed the retention samples and following any full investigation of the Manufacturing process it conducts, shall be final and determinative. If the Third Party Laboratory determines that the retained samples meet the Specifications, the rejection by Distributor is deemed to be unjustified, and Distributor shall promptly pay Can-Fite for any replacement Product. If the Third Party Laboratory determines that the relevant shipment of Supplied Product does not meet the Specifications, Can-Fite shall not invoice Distributor for the replacement Supplied Product. The Party against whom the Third Party Laboratory rules shall also bear the fees charged by the Third Party Laboratory in connection with resolution of the disagreement, including all out-of-pocket costs of investigating the Manufacturing process.

(d) At Can-Fite's election and upon authorization from Can-Fite, Distributor shall destroy the rejected Supplied Product promptly and provide Can-Fite with certification of such destruction unless Can-Fite elects to have the Supplied Product returned, in which event Distributor shall cooperate in arranging such return. If Can-Fite agrees with the basis for Distributor's rejection or if the Third Party Laboratory rules against Can-Fite, Can-Fite shall pay the cost of destroying or returning the Supplied Product. In all other cases, Distributor shall bear such costs.

(e) Notwithstanding any of the other provisions in this Agreement and without limiting any other provision herein, Distributor agrees that the remedies set forth in this Section 6.6 are Distributor's sole and exclusive remedies with respect to the rejection of Supplied Product.

6.7 Prices and Payments.

(a) Subject to the provisions of Section 6.3 hereof, Distributor shall pay to Can-Fite or Can-Fite's designees the following:

(i) The Milestone Payments in the amounts and at the time as set out in Part A of Schedule C;

(ii) The Transfer Price for Supplied Product supplied by Can-Fite in the amounts calculated in accordance with the provisions of Part B of Schedule C;

(iii) Royalty payments calculated in accordance with the provisions of Part C of Schedule C; and

(iv) The share of the Net Profits from Distributor's sale of an Authorized Generic in accordance with Section 2.4.

(b) Distributor shall pay all insurance and shipping costs and any Taxes imposed on the importation of Supplied Product into the Territory.

(c) Distributor shall be responsible for the payment of any duties, levies or Taxes applied to the sale of Supplied Product in the Territory by any relevant Tax authority.

(d) Any payments to be made hereunder and which have not been made by the due date, shall accrue interest at any monthly rate equal to [...]. Additionally, Distributor shall be responsible for all reasonable attorneys' fees, witness fees and court costs and other costs incurred by Can-Fite to recover amounts owing to it hereunder.

(e) Distributor shall make all payments contemplated by this Agreement in the lawful currency of Canada and Distributor shall make such payments to such address as Can-Fite may from time to time direct in writing to Distributor.

6.8 Audit.

Distributor shall keep and retain complete and accurate records pertaining to the disposition of Supplied Product and amounts payable under this Agreement (including, without limitations, amounts payable pursuant to Section 2.4 hereof) for each Fiscal Year or part thereof during the Term in sufficient detail to permit Can-Fite to confirm the accuracy of all payments made or due hereunder for a period of three (3) years following the applicable Fiscal Year or part thereof. At Can-Fite's request, Can-Fite and Distributor shall jointly appoint an independent internationally recognized audit firm to audit the books of account of Distributor in order to determine whether Distributor has properly reported and accounted for any fees or payments due to Can-Fite pursuant to this Agreement. The appointed audit firm may perform audits during regular business hours, not more than once in any calendar year during the Term and upon reasonable prior notice to Distributor. Can-Fite shall bear the audit fees unless such audit firm determines that the amount actually due Can-Fite, in the aggregate, exceeds the amounts paid or deemed paid by Distributor hereunder by [...], in which case Distributor shall bear the audit fees. Distributor shall forthwith pay any amounts discovered to be due pursuant to an audit together with interest from the date payment was originally due at a monthly rate equal to [...]. The results of the audit shall be final and binding upon the Parties.

6.9 Facility Audits.

(a) Distributor and/or its nominee shall have the right to conduct an audit of any Approved Manufacturing Site(s) at which the Supplied Product is being Manufactured, of Manufacturing records relating to the production of such Product, if applicable, of the Contract Finisher(s)' facility where Supplied Product is Packaged and of any correspondence between Can-Fite and the Regulatory Authority related to such Supplied Product or such facilities, during business hours upon ten (10) Business Days prior written notice to Can-Fite not more than once per Fiscal Year during the Term of this Agreement, unless either Party, any Authority or any Third Party raises any questions about the quality of the Supplied Product which could have a material detrimental effect on the sales or use of Supplied Product, in which case Distributor's audit right shall not be subject to the foregoing limitation until the specific issue in question has been resolved, and Can-Fite shall promptly supply or cause its Approved Manufacturer to supply to Distributor all data and results relating to all Testing performed in connection with the issue in question.

(b) Can-Fite and/or its nominee shall have the right to conduct an audit of the facilities and records of Distributor and/or its SubDistributors and/or their Affiliates relating to the Marketing, Testing, and storage of Supplied Product and of any correspondence between Distributor and/or its SubDistributors and/or their Affiliates and the Regulatory Authority related to Supplied Product or such facilities, during business hours upon ten (10) Business Days prior written notice to Distributor not more than once per Fiscal Year during the Term of this Agreement, unless any Authority or any Third Party raises any questions about the quality of the Supplied Product or the Testing and Marketing thereof which could have a material detrimental effect on the sales or use of Supplied Product, in which case Can-Fite's audit right shall not be subject to the foregoing annual limitation until the specific issue or question has been resolved, and Distributor shall promptly supply to Can-Fite all data and results relating to all Testing performed by Distributor on Supplied Product.

7. INTELLECTUAL PROPERTY

7.1 Ownership of Can-Fite Intellectual Property.

Can-Fite shall retain all of its rights, title and interest in and to all Product Technology, Can-Fite Trademarks, copyrights, and all other industrial and Intellectual Property embodied in or which covers the Product, in each case which is owned, held, or licensed by it as of the Effective Date or thereafter or developed, created or discovered by it or on its behalf during the Term, subject to the rights granted in this Agreement. Except as otherwise expressly provided in this Agreement, Distributor has and shall have no right, title or interest in any Intellectual Property owned by or licensed to Can-Fite relating to the Product including the Product Technology and Can-Fite Trademarks.

7.2 Ownership of Distributor Intellectual Property.

Distributor shall retain all of its right, title and interest in and to all copyrights and all other Intellectual Property owned, held, or licensed by it as of the Effective Date or thereafter developed, created or discovered by it or on its behalf during the Term, including Trademarks. For clarification purposes, the Parties agree that nothing herein grants, or constitutes an agreement or obligation to grant, to Can-Fite, any Approved Manufacturer or any of their Affiliates or other Third Party any right, title or interest in, to or under any of the Trademarks.

7.3 Maintenance and Prosecution of Product Patents.

As between Distributor and Can-Fite, Can-Fite shall remain responsible for maintenance of Product Patents and shall bear all expenses associated therewith including prosecution, renewal and other fees necessary to obtain and maintain the Product Patents in full force and effect until the earlier of their expiration or the termination or expiration of this Agreement.

7.4 Notice of Patent Infringement.

(a) Information Concerning Infringement. If either Party shall learn of (i) any claim or assertion that the Manufacture, Marketing, Packaging or Testing of the Supplied Product, or the use of the Product Technology or other Intellectual Property related to the Supplied Product infringes, misappropriates or otherwise violates the Intellectual Property rights of any Third Party, or (ii) the actual or threatened infringement, misappropriation or other violation by any Third Party of the Product Technology or other Intellectual Property related to the Product, then the Party becoming so informed shall as soon as reasonably practicable, but in all events within ten (10) Business Days thereof, notify the other Party of such claim or assertion, or actual or threatened infringement, misappropriation or other violation.

(b) Potential Infringement. In the event either Can-Fite or Distributor learns of any Third Party patents which may cover the Manufacturing, Marketing, Testing or Packaging of the Supplied Product in the Territory, such Party will promptly notify the other Party. The Parties agree to confer in good faith regarding such potential infringement risk and to explore reasonable alternatives for avoiding such risk and to provide such information to each other as either Party may reasonably request.

(c) Third Party Claims; Defense by Can-Fite. If a Third Party files or threatens to file a claim, suit or action against Can-Fite or Distributor claiming that a patent or other Intellectual Property right held by or licensed to it is infringed, misappropriated or otherwise violated by the Manufacturing, Marketing or Testing or Packaging of the Supplied Product, and such claim, suit or action arises out of Distributor's exercise of its rights under this Agreement, the Parties shall confer in good faith regarding such alleged infringement, misappropriation or other violation. Can-Fite may, but shall not be obligated to, defend any such claims, suits or actions and shall notify Distributor of its election within thirty (30) days of receipt of notice. If Can-Fite elects to defend such claims, suits or actions, it shall notify Distributor that it has elected to do so. Can-Fite shall provide information to Distributor of the conduct of the defense of such claims, suits or actions as Distributor may reasonably request from time to time. Distributor will assist in the defense of any such claim, suit or action as reasonably requested by Can-Fite. Can-Fite and Distributor shall be equally responsible for and pay any payments made to Third Parties, and shall share equally all fees, costs and expenses (including, without limitation, outside attorneys' fees and expenses of Distributor and Can-Fite) as a result of any actual or alleged infringement. Can-Fite shall not settle any such claim, suit or action if such settlement would impose on Distributor the obligation to pay or contribute to any claim, without the prior express written consent of Distributor, which shall not be unreasonably withheld, conditioned, or delayed. The Parties agree that in the event Can-Fite fails to remit any payments required to be made to Third Parties or related expenses as provided above, and Distributor, in its sole discretion, elects to make such payments, Distributor may set off such amounts against the payments to be made by Distributor to Can-Fite pursuant to Section 6.7(a).

(d) Defense by Distributor. If Can-Fite elects not to defend against Third Party claims, suits or actions pursuant to Section 7.4(c), Can-Fite shall give notice of its decision to Distributor within reasonably sufficient time to permit Distributor, at its option and without requirement, to defend against such claims, suits or actions. If Distributor, in its sole discretion, elects to defend such Third Party claims, suits or actions, it shall notify Can-Fite that it has elected to do so and shall notify Can-Fite in writing of its proposed legal counsel. Distributor shall provide information to Can-Fite of the conduct of the defense of such claims, suits or actions as Can-Fite may reasonably request from time to time and Can-Fite shall assist in such defense as reasonably requested by Distributor. Can-Fite and Distributor shall be equally responsible for and pay any payments made to Third Parties and shall share equally all fees, costs and expenses (including, without limitation, outside attorneys' fees of Distributor and Can-Fite) as a result of any actual or alleged infringement. The Parties agree that in the event Can-Fite fails to remit any payments required to be made to Third Parties or related expenses, Distributor may set off such amounts against the payments to be made by Distributor to Can-Fite pursuant to Section 6.7(a). Distributor shall not settle any such claim, suit or action if such settlement would impose on Can-Fite the obligation to pay any claim, without the prior express written consent of Can-Fite, which shall not be unreasonably withheld, conditioned, or delayed.

7.5 Can-Fite Trademarks Indemnified Infringement Claims.

Can-Fite agrees that it shall, at its own cost and expense, defend, indemnify and hold harmless the Distributor Indemnitees from and against any and all liabilities, losses, damages, actions, claims and expenses suffered or incurred by Distributor Indemnitees (including reasonable attorneys' fees, court costs and expert witnesses' fees) (collectively "**Claims**") arising out of, resulting from or otherwise related to the Can-Fite Trademarks used by any Distributor Indemnitee as permitted by this Agreement, provided that any such Claim does not arise from Distributor's breach of this Agreement, or arise from Distributor Indemnitee's negligent or intentionally wrongful conduct. The Parties agree that nothing in this Section 7.5 limits Can-Fite's obligations to bear an equal share of any payments made to Third Parties as provided under Section 7.4(c) or Section 7.4(d) or indemnity obligations under Article 10 of this Agreement).

7.6 Trademarks Indemnified Infringement Claims.

Distributor shall, at its own cost and expense, defend, indemnify and hold harmless the Can-Fite Indemnitees from and against any and all Claims suffered or incurred by Can-Fite Indemnitees (including reasonable attorneys' fees, court costs and expert witnesses' fees) arising out of, resulting from or otherwise related to the Trademarks used by Distributor, its Affiliates, sublicensees, SubDistributors or agents, other than the Can-Fite Trademarks, provided that any such Claim does not arise from Can-Fite's breach of this Agreement, or arise from Can-Fite Indemnitee's negligent or intentionally wrongful conduct. The Parties agree that nothing in this Section 7.6 limits Distributor's obligations to bear an equal share of any payments made to Third Parties as provided under Section 7.4(c) or Section 7.4(d) or indemnity obligations under Article 10 of this Agreement).

7.7 Infringement of Product Technology by a Third Party.

(a) In the event that any Party becomes aware of any Person infringing or potentially infringing the Product Technology in the Territory, whether by direct or indirect infringement, or by misappropriation of Product Technology, it shall promptly notify the other Party. Distributor shall not give notice (written or other) of infringement of any of the Product Technology or infringement or misappropriation of other Intellectual Property of Can-Fite to any Third Party without Can-Fite's prior written consent; *provided, however*, that Distributor may give such notice to a Third Party without Can-Fite's consent but upon thirty (30) days prior written notice to Can-Fite, if (a) Can-Fite has declined to take steps to abate such infringement or misappropriation and Distributor has the right to enforce the Product Technology or other Intellectual Property of Can-Fite against such Third Party infringer as set forth in this Article 7; or (b) disclosure is required by applicable Laws to which Distributor is subject. In a case where Distributor receives a notice of allegation under the *Patented Medicines (Notice of Compliance) Regulations* in respect of the Product Patents, Can-Fite shall use Commercially Reasonable Efforts (including financial assistance) to assist Distributor in seeking an order, within the forty-five (45) day deadline required under the *Patented Medicines (Notice of Compliance) Regulations,* prohibiting Health Canada from issuing a notice of compliance for a Third Party's drug product until the expiration of the Product Patents that are the subject of such notice of allegation. For any actions other than those under the *Patented Medicines (Notice of Compliance) Regulations,* unless the Parties otherwise mutually agree in writing, Can-Fite shall have the initial right, but not the obligation to enforce the Product Technology or defend any declaratory action with respect thereto (an "**Enforcement Action**"), at its expense and using its Commercially Reasonable Efforts, and Distributor shall give all reasonable assistance (excluding financial assistance) to Can-Fite in such Enforcement Action. However, if (i) Can-Fite agrees in writing not to bring or defend an Enforcement Action with respect to any Product Technology in the Territory or (ii) within ninety (90) days following a written request by Distributor to do so and confirmation of facts reasonably supporting existence of such actual or suspected infringement with respect to Product Technology in the Territory for which Distributor has license rights under this Agreement, Can-Fite fails to bring or defend an Enforcement Action or take other commercially reasonable action to protect the Product Technology from such infringement, or to abate such infringement, then Distributor shall have the right, but not the obligation, at its sole discretion, to institute an Enforcement Action in its own name at its own expense, and with the right to control the course of such Enforcement Action (and Can-Fite shall provide all reasonable assistance to Distributor for such Enforcement Action, at Distributor's expense, including joining such Enforcement Action if necessary to maintain the Enforcement Action, and Can-Fite shall have the right to join and participate in the Enforcement Action whether or not such joinder is requested by Distributor; if not requested by Distributor, such participation will be at Can-Fite's expense). Any amounts recovered with respect to any Enforcement Action pursuant to this Section 7.7(a) shall be applied first to reimburse the Parties for their reasonable out-of-pocket expenses (including reasonable attorneys' fees) in the prosecution of such infringement. The remainder shall be deemed Net Sales. Notwithstanding any provision to the contrary, Distributor shall not be precluded from seeking, in its own independent cause of action, the recovery of damages resulting from its own lost sales, price erosions or similar damages suffered or incurred by Distributor.

7.8 Trademarks.

(a) License. Subject to the terms and conditions of this Agreement, Can-Fite hereby grants to Distributor an exclusive right for use in the Field within the Territory to use the Can-Fite Trademarks solely for the purposes of Marketing the Products under this Agreement. Such license shall not preclude Can-Fite and/or any Approved Manufacturer from using Can-Fite Trademarks within the Territory for any Product that is to be Marketed or sold outside the Territory.

(b) No Obligation to Use Trademarks. Distributor may use the Can-Fite Trademarks solely for the Marketing of the Products for use in the Field in the Territory. Distributor may use its own Trademarks on Product Packaging, brochures and other promotional materials to identify itself as the distributor of the Product provided that Distributor has obtained the applicable Regulatory Approval.

(c) Can-Fite Ownership. Distributor hereby agrees to and recognizes Can-Fite's exclusive ownership or license rights of the Can-Fite Trademarks and the renown of the Can-Fite Trademarks. Distributor agrees not to take any action inconsistent with such ownership and further agrees to take any action, at Can-Fite's expense, which Can-Fite reasonably deems necessary to establish and preserve Can-Fite's exclusive rights in and to the Can-Fite Trademarks including cooperating in the registration of the Can-Fite Trademarks on the trademark registry or other appropriate registration procedure in each jurisdiction in the Territory.

(d) Distributor Ownership. Can-Fite hereby agrees to and recognizes Distributor's exclusive ownership or license rights of the Trademarks and the renown of the Trademarks. Can-Fite agrees not to take any action inconsistent with such ownership and further agrees to take any action, at Distributor's expense, which Distributor reasonably deems necessary to establish and preserve Distributor's exclusive rights in and to the Trademarks including cooperating in the registration of the Trademarks on the trademark registry or other appropriate registration procedure in each jurisdiction in the Territory.

(e) Can-Fite Goodwill. The Parties agree that all use of the Can-Fite Trademarks by Distributor shall be for the sole and exclusive benefit of Can-Fite and the goodwill and reputation accrued in connection with Distributor's or its Affiliates' or SubDistributors' use of the Can-Fite Trademarks shall accrue solely to Can-Fite. In the event Distributor acquires any right, title or interest in or to or relating to the Can-Fite Trademarks for any reason, Distributor shall immediately assign or cause to be assigned (in the case of Distributor's Affiliates) at no cost to Can-Fite, all such right, title and interest, together with any related goodwill or reputation, to Can-Fite. Distributor or its Affiliates shall promptly execute all documents reasonably requested by Can-Fite in connection with such assignment and shall use commercially reasonable efforts to cause its SubDistributors to do the same.

(f) Distributor Goodwill. The Parties agree that all use of the Trademarks by Distributor and its Affiliates and SubDistributors shall be for the sole and exclusive benefit of Distributor, and the goodwill and reputation accrued in connection with Distributor's or any Affiliate's or SubDistributor's use of the Trademarks shall accrue solely to Distributor. The Parties agree that Can-Fite and its Affiliates will have no rights to use (or to authorize the use by any Third Party) any of the Trademarks. Notwithstanding the foregoing, in the event Can-Fite, or any of its Affiliates acquires any right, title or interest in or to or relating to the Trademarks for any reason, Can-Fite shall immediately assign, or cause to be assigned (in the case of Can-Fite's Affiliates), at no cost to Distributor, all such right, title and interest, together with any related goodwill or reputation, to Distributor. Can-Fite or its Affiliates shall promptly execute all documents reasonably requested by Distributor in connection with such assignment.

(g) Infringement. Distributor agrees that only Can-Fite has the right to enjoin any infringement or registration by a Third Party of the Can-Fite Trademarks, provided, however, that Can-Fite may authorize Distributor to enjoin such infringement or registration. Distributor will assist in the prosecution of any such action as reasonably requested by Can-Fite at Can-Fite's cost. Notwithstanding the foregoing, Can-Fite at it sole cost and expense will diligently enforce the Can-Fite Trademarks in the Territory for the benefit of Distributor.

(h) No Confusion. Distributor shall not adopt, use, or register any acronym, trademark, trade names, service mark or other marketing name that is confusingly similar to or dilutive of the Can-Fite Trademarks or the Can-Fite name, and shall not use the Can-Fite Trademarks or the Can-Fite name other than in connection with the Marketing of the Product pursuant to this Agreement. Can-Fite shall not adopt, use, or register any acronym, trademark, trade names, service mark or other marketing name that is confusingly similar to or dilutive of the Trademarks or the Distributor name, and shall not use the Trademarks or the Distributor name other than in connection with the Manufacturing and Testing of the Product pursuant to this Agreement.

8. CONFIDENTIALITY

8.1 Can-Fite's Information.

Except as provided in Section 8.3 or elsewhere in this Agreement, Distributor shall maintain all of Can-Fite's Confidential Information provided by Can-Fite to Distributor, whether in writing, electronically, orally or through access to Can-Fite's premises, in strict confidence. Such information shall remain the property of Can-Fite, and Distributor shall not use the same for or on behalf of any Person or entity other than Can-Fite or make use of any such information except as permitted by this Agreement without the express prior written approval of Can-Fite.

8.2 Distributor's Information.

Except as provided in Section 8.3 or elsewhere in this Agreement, Can-Fite shall maintain all of Distributor's Confidential Information provided by Distributor to Can-Fite, whether in writing, electronically, orally or through access to Distributor's premises, in strict confidence. Such information shall remain the property of Distributor, and Can-Fite shall not make use of any such information except as permitted by this Agreement without the express prior written approval of Distributor.

8.3 Exceptions.

The covenants of the receiving Party contained in Section 8.1 and Section 8.2 shall not apply to Confidential Information (a) that the receiving Party can reasonably demonstrate by competent proof is required to be disclosed by Law or a court or other Authority pursuant to (i) regulatory filings; (ii) prosecuting or defending litigation; (iii) complying with applicable Law and orders or decisions of any Official Body having jurisdiction; (iv) necessary to the limited extent only to conducting pre-clinical or clinical trials of Product and persons involved in such trials are bound by similar terms of confidentiality; or (b) disclosed to directors, officers, employees, representatives, or Affiliates who agree to be bound by similar terms of confidentiality. Notwithstanding any provision herein to the contrary, nothing herein shall prevent or prohibit any disclosure of any information concerning this Agreement (A) required under applicable securities Laws and the rules and regulations of any stock exchange or market system on which any Party's securities are or may be traded, (B) by either Party in connection with an Approved Transaction (as defined below), where prospective parties or the other party or parties to such Approved Transaction have entered into confidentiality agreements with the Party concerning such Confidential Information, (C) to either Party's financial advisors or legal advisors who have agreed to the limitations on disclosure contained herein and/or (D) to investment bankers and/or financing sources in connection with *bona fide* financing transactions involving either Party or an Affiliate. For the purposes of this Agreement, each of the following shall constitute an "**Approved Transaction**": (i) the issuance by either Party of securities in connection with any financing transaction or public offering, and/or (ii) a merger, consolidation or other similar transaction involving either Party (i.e., wherein another entity acquires all or substantially all of that Party's equity interests or assets or a merger or consolidation or similar transaction wherein securities of the post transaction entity will be issued to the other party). If a Party is required or permitted to make a disclosure of the other Party's Confidential Information pursuant to this Section 8.3, it will use commercially reasonable efforts to (I) limit the scope of the Confidential Information disclosed and the number of persons to whom such Confidential Information is disclosed, in each case to the minimum extent required to address the reason such disclosure is permitted hereunder and (II) secure confidential treatment of such Confidential Information and comply with any applicable provisions of Section 12.7.

8.4 Publications.

A Party primarily responsible for a proposed publication (excluding any publication required under applicable securities Laws, which shall be subject to the provisions of Sections 8.3 and 12.7) relating to the Product in the Territory (the primary purpose of which is not advertising or promotion), whether written or oral, shall, at least thirty (30) days before presentation or submission of the proposed publication to a Third Party, submit such proposed publication to the other Party for review in connection with obtaining or preserving Intellectual Property rights and/or to determine whether such other Party's Confidential Information is contained therein and should be modified or deleted. The receiving Party shall have thirty (30) days in which to review and consent to each proposed publication, such consent not to be unreasonably withheld or delayed. The Parties may mutually agree to extend the review period for an additional thirty (30) days when the receiving Party provides a reasonable need for such extension, including, but not limited to the preparation and filing of pertinent patent applications.

8.5 Survival.

This Article 8 shall survive termination of this Agreement for a period of three (3) years.

9. TERM AND TERMINATION OF AGREEMENT

9.1 Term.

The term of this Agreement shall commence on the Effective Date and continue for fifteen (15) years from the date of the First Commercial Sale (the "**Initial Term**"). This Agreement will be automatically renewed for 5 (five) year periods (each a "**Renewal Term**" and together with the Initial Term, the "**Term**") unless either Party gives to the other Party notice of termination at least six (6) months prior to the expiry of the then current Term.

9.2 Termination.

(a) Material Breach. Except as expressly specified in this Section 9.2, this Agreement may not be terminated for a breach or otherwise, provided however, that a Party may seek to recover damages for a breach, whether or not cured, and a Party may seek specific performance for any breach of this Agreement.

(b) Distributor's Termination Rights. Distributor may terminate this Agreement:

(i) at any time following receipt of the Regulatory Approval on ninety (90) days' prior written notice to Can-Fite;

(ii) if Can-Fite (through itself or its Affiliates) breaches its obligations under Section 2.3 such termination shall be effective upon thirty (30) days prior written notice of termination sent by Distributor to Can-Fite, provided however, that Can-Fite shall have thirty (30) days from the date of such notice to cure such breach; and such cure may be effected by cessation of the activities causing the breach and termination of any licenses or rights granted to Third Parties in breach of Section 2.3;

(iii) if a Supply Interruption occurs and Can-Fite is not able to resume supply as set forth in Section 6.3(c).

(c) Can-Fite's Termination Rights. Can-Fite may terminate this Agreement:

(i) If Distributor fails to pay any amounts due to Can-Fite under this Agreement in excess of $20,000 (due and owing at one time) when due; provided however, such amounts are not subject to setoff as provided in Section 12.2; and provided further, such payments are not subject to a bona fide dispute; provided, further, that if Distributor pays the amounts due and payable pursuant to Section 6.7(a)(iii) or (iv), in each case, in accordance with Distributor's good faith calculations, and Can-Fite disagrees with those calculations and/or requests an audit with respect to such calculations, any amounts in excess of such good faith calculations shall be payable pursuant to clause (B) of the following sentence. Such termination shall be effective, (A) in the case of (I) failure to make payments not subject to a bona dispute or (II) failure of Distributor to make payments under Sections 6.7(a), in each case, to the extent of Distributor's good faith calculations, upon ten (10) days prior written notice of termination sent by Can-Fite to Distributor, provided that Distributor shall have (10) ten days from receipt of notice of termination to cure such default, and (B) in the case of all other payment defaults ten (10) days following Distributor's receipt of written notice of termination provided by Can-Fite sent after resolution of the payment dispute (by agreement between the Parties, through the mechanism of Section 6.8, or through the mechanism of Section 12.2, as applicable). provided however that Distributor shall have ten days from receipt of such notice of termination to cure such default;

(ii) if Distributor or its Affiliates breaches its obligations under Sections 2.2, 2.3 or 8, such termination shall be effective upon thirty (30) days prior written notice of termination sent by Can-Fite to Distributor, provided however, that Distributor shall have thirty (30) days from the date of such notice to cure such breach; and such cure may be effected by the immediate cessation of the activities causing the breach and termination of any licenses or rights granted to Third Party in breach of such Section 2.2 or 2.3;

(iii) if First Commercial Sale is not achieved within one year from the NDS; provided, however, that Can-Fite shall not be entitled to terminate this Agreement if failure to achieve such First Commercial Sale results from a failure of Can-Fite to supply Product or another circumstance beyond the control of Distributor, including, without limitation, a Force Majeure or a change in applicable Law; or

(iv) in the event the minimum sales requirements set forth in Schedule D are not achieved.

(d) Bankruptcy and Insolvency. A Party shall have the right to terminate this Agreement in the event that a court of competent jurisdiction declares the other Party insolvent or bankrupt, or a bankruptcy proceeding is commenced against the other Party that is not dismissed within ninety (90) days of commencement or the other Party files a proposal, assignment for the benefit of creditors, arrangement, composition or seeks similar relief under any applicable bankruptcy law or the other Party is in receivership, in which case termination shall be effective upon written notice to that effect.

9.3 Accrued Rights, Surviving Obligations.

Termination or expiration of this Agreement shall not affect any accrued rights of either Party or payments otherwise owing. Without limiting the foregoing, the terms of Sections 4.8, 5.1, 5.2, 5.3, 5.4, 6.7 (to the extent of amounts owed that accrued during the Term and amounts owed for sale of unsold Product (percentage of Net Sales) and unsold Authorized Generic (percentage of Net Profits) under Section 9.4), 6.8 and 6.9 (only with respect to specific issues relating to quality of Supplied Product delivered to Distributor during the Term) and Articles 7 (excluding Section 7.7 with respect to actions commenced post-termination, but including such section for actions commenced pre-termination (but only to the extent of pre-termination infringement, with any damages for post-termination infringement, accruing only to Can-Fite (as opposed to Distributor) and with Distributor having no obligation to pursue such post-termination damages) and except that the provisions of Section 7.4 shall survive only to the extent a claim, suit or action arises out of Distributor's exercise of rights under this Agreement), 8, 9, 10, 11, and 12 of this Agreement shall survive termination or expiration of this Agreement.

9.4 Transitional Matters.

(a) Upon expiration or termination of the Agreement, Distributor may, where permitted by Law, sell Supplied Product then in its inventory for a period of [...] months thereafter, all in accordance with the terms of this Agreement. [...]. Can-Fite will have the right to cancel any purchase orders placed by Distributor which were accepted by Can-Fite prior to such termination, and which require delivery of Supplied Product after the date of termination including during such twelve (12) month period.

(b) Upon termination, Distributor and Can-Fite shall at their own expense make Commercially Reasonable Efforts to ensure that the continuity of patient care is not disrupted including transferring of managed care contracts, adverse event reporting, and dealing with supply chain matters. In addition, Distributor will remain responsible for returned Supplied Product sold by Distributor and Can-Fite will be responsible for returned Supplied Product following termination of this Agreement provided it was not sold by Distributor pursuant to this Agreement, including Section 9.4(a) above. For the purpose of identifying the responsible party, Supplied Product will be tracked via lot numbers.

9.5 Transfer of Approvals.

Within thirty (30) days of expiration or termination of the Agreement, Distributor shall transfer or cause to be transferred to Can-Fite, or to any Third Party designated by Can-Fite, all Approvals relating to Supplied Product, including all Regulatory Approvals, the New Drug Submission(s), Other Approvals, and Can-Fite Trademarks and Trademarks specifically relating to the Product or Authorized Generic, or applications therefore, that are in the name of Distributor, at Can-Fite's cost.

9.6 Effect of Termination.

Termination of this Agreement shall not operate to release either Party from any obligation or liability incurred under this Agreement prior to or upon termination hereof or which, by the terms hereof, survives termination. Upon any termination of this Agreement, except to the extent required for the purposes of Section 9.4, (i) all licenses and rights granted to Distributor hereunder shall immediately terminate and (ii) all rights, properties and interests granted by Can-Fite to Distributor shall immediately revert to and become fully vested in Can-Fite and Distributor shall return to Can-Fite all copies of documents regarding Supplied Product and all Confidential Information supplied by Can-Fite. For the avoidance of doubt, the Parties acknowledge that Can-Fite shall have no rights to the Trademarks following any termination of this Agreement.

9.7 License Survival During Bankruptcy.

The Parties agree that Distributor, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Israeli bankruptcy law subject to performance by Distributor of its obligations under this Agreement. The parties further agree that, in the event Can-Fite elects to reject or terminate this Agreement while Can-Fite is the subject of a case or proceeding for bankruptcy and Distributor elects to continue the licenses under this Agreement as contemplated by the preceding sentence, then Distributor shall be entitled, upon reasonable request, to have access, in confidence, to such of Product Know How not already in Distributor's possession, as shall be reasonably necessary to make use of the license rights under this Agreement without participation by Can-Fite, subject to the terms and conditions of this Agreement, including without limitation, Sections 2.2, 2.3 and 2.4. The licensor of intellectual property to Distributor under this Agreement shall be (i) an Israeli entity or (ii) an entity of a jurisdiction having legal protections in the event of a bankruptcy or reorganization filing of the licensor, which in the reasonable opinion of Distributor, are comparable or at least as favorable to a licensee as those provided under Section 365(n) of the U.S. Bankruptcy Code, as in effect as of the Effective Date; provided, however, if the licensor is not an entity of the type contemplated in clauses (i) and (ii) above, then licensor shall place its intellectual property rights which relate to this Agreement in a trust or other structure which will provide protection to the licensee in the event of the bankruptcy or reorganization filing of the licensor at a level at least comparable to that contemplated in clauses (i) or (ii) above; and provided, further, that such trust or similar structure must be reasonably acceptable to Can-Fite and Distributor.

10. INDEMNITY

10.1 Indemnification by Can-Fite.

Can-Fite agrees to and hereby does indemnify, defend and hold the Distributor Indemnitees harmless from and against all losses, claims, damages, costs and expenses, including reasonable attorneys' fees (including, without limitation, those resulting from Third Party claims, actions, or proceedings) (collectively "**Losses**") arising from: (a) the breach of any representation, warranty, covenant or obligation by Can-Fite hereunder (except for that relating to Third Party infringement indemnification, the provisions for which are exclusively limited to Sections 7.4 and 7.5), (b) any negligent act or omission, or willful misconduct of Can-Fite or its Affiliates or any of its Approved Manufacturers or, as applicable, any of its Contract Finishers; (c) the Marketing of Supplied Product inside or outside the Territory by Can-Fite or any of its Affiliates; (d) the failure of the Supplied Product sold to Distributor to meet the Specifications; or (e) any Product Liability Claims, not covered by subsections (a)-(d) above or subsections (a)-(g) of Section 10.2 (to the extent of fifty percent (50%) of such Losses); provided, however, that in the case of each of subsections 10.1(a), (c), (d), or (e) Can-Fite shall have no indemnity obligation to Distributor for any Losses for which Distributor is obligated to indemnify Can-Fite pursuant to Section 10.2 if the Losses are primarily and substantially a result of the facts giving rise to Distributor's obligation to indemnify.

10.2 Indemnification by Distributor.

Distributor agrees to and hereby does indemnify and hold the Can-Fite Indemnitees harmless from and against all Losses (unless other specified) arising from: (a) the Marketing, Testing, sale or other distribution of Supplied Product by Distributor or its SubDistributors or any of their respective Affiliates or agents in violation of the terms of this Agreement; (b) breach of any representation, warranty, covenant or obligation by Distributor hereunder; (c) any negligent act or omission, or willful misconduct of Distributor or its SubDistributors or any of their respective Affiliates or agents (d) sale or use of a pharmaceutical product which is not supplied by or on behalf of Can-Fite or any of its Approved Manufacturers or any of their respective Affiliates or agents pursuant to this Agreement and which is sold or combined by Distributor or any SubDistributor with Supplied Product, (e) improper handling, storage or transport of Supplied Product by Distributor, its Affiliates, or any SubDistributor or their respective agents, (f) the unauthorized alteration, modification, or adulteration of Supplied Product by Distributor, its Affiliate, or any SubDistributor, (g) any representations or warranties made by Distributor or any of its Affiliates or SubDistributors with respect to Supplied Product (other than the labeling approved by the Regulatory Authority), or (h) any Product Liability Claims, not covered by subsections (a)-(d) of Section 10.1 or subsections (a)-(g) of this Section 10.2 (to the extent of fifty percent (50%) of such Losses), provided, however, that in the case of each of subsections 10.2(a)-(c) and (e)-(g), Distributor shall have no indemnity obligation to Can-Fite for any Loss for which Can-Fite is obligated to indemnify Distributor pursuant to Section 10.1 if the Losses are primarily and substantially a result of the facts giving rise to Can-Fite's obligation to indemnify.

10.3 Procedure.

This Section 10.3 describes the procedure for indemnification of Losses for Third Party claims. With respect to Losses relating to the claim of a Party hereto, the procedures provided in Section 12.2 shall govern. The Party seeking indemnification for Third Party claims under Sections 10.1 or 10.2 (the "**Indemnified Party**") shall promptly notify the other Party (the "**Indemnifying Party**") in writing of all matters which may give rise to the right to indemnification hereunder; *provided, however*, that failure to promptly give the notice provided in this Section 10.3 shall not be a defense to the liability of the Indemnifying Party for such claim, but the Indemnifying Party may recover any actual Losses arising from the Indemnified Party's failure to give such prompt notice. The Indemnified Party shall not admit any liability with respect to, or settle, compromise or discharge any such matter covered by this Article 10 without the Indemnifying Party's prior written consent (which shall not be unreasonably withheld, delayed or conditioned). The Indemnifying Party shall have the right, with the consent of the Indemnified Party (which shall not be unreasonably withheld, delayed or conditioned), to settle all indemnifiable matters under this Article 10 related to claims by Third Parties which are susceptible to being settled. In connection with any claim giving rise to indemnity under this Article 10 resulting from or arising out of any claim or legal proceeding by a Person other than the Indemnified Party, the Indemnifying Party at its sole cost and expense may, upon written notice to the Indemnified Party and an acknowledgement of its indemnity obligations hereunder, assume the defense of any such claim or legal proceeding. If the Indemnifying Party assumes the defense of any such claim or legal proceeding, the Indemnifying Party shall select counsel reasonably acceptable to the Indemnified Party to conduct the defense of such claims or legal proceedings and, at the Indemnifying Party's sole cost and expense (which costs and expenses shall not be applied against any indemnity limitation herein), shall take all steps necessary in the defense or settlement thereof. The Indemnified Party shall be entitled to participate in (but not control) the defense of any such action, with its own counsel and at its own expense, and shall be entitled to any and all information and documentation relating thereto. If the Indemnifying Party does not assume (or continue to diligently and competently prosecute) the defense of any such claim or litigation resulting therefrom in accordance with the terms hereof, the Indemnified Party may, at the Indemnifying Party's expense, defend against such claim or litigation in such manner as it may deem appropriate, but may not settle such claim or litigation without the consent of the Indemnifying Party, which consent shall not be unreasonably withheld, delayed or conditioned. The Indemnified Party will cooperate reasonably with the Indemnifying Party in its efforts to conduct or resolve such matters, including by making available to the Indemnifying Party relevant documents and witnesses. The Indemnified Party and the Indemnifying Party shall keep each other informed of all settlement negotiations with Third Parties and of the progress of any litigation with Third Parties. The Indemnified Party and the Indemnifying Party shall permit each other reasonable access to books and records and shall otherwise cooperate with all reasonable requests of each other in connection with any indemnifiable matter resulting from a claim by a Third Party.

10.4 Indemnification Not Sole Remedy.

Each Party hereby acknowledges that the indemnification provided under this Article 10 shall in no manner limit, restrict or prohibit (unless liability is otherwise expressly limited by the terms of this Agreement) either Party from seeking any recovery or remedy provided at law or in equity from the other Party in connection with any breach or default by such other Party of any representation, warranty or covenant hereunder, including injunctive relief.

10.5 Insurance.

Each Party will have in force prior to the First Commercial Sale and shall maintain in good standing throughout the Term of this Agreement and for a period of seven (7) years thereafter, product liability insurance policies in respect of the Supplied Product(s) with an internationally recognized insurer or insurers licensed to do business in the Territory in an amount not less than $5 million per occurrence, on such terms and conditions as are customary in the industry, and shall list the other Party as an additional insured on such policy(ies). Each Party shall provide proof of such insurance to the other Party within ten (10) days prior to the First Commercial Sale and thereafter from time to time within thirty (30) days of request of proof of such insurance.

11. REPRESENTATIONS, WARRANTIES AND COVENANTS; LIMITATIONS OF LIABILITY

11.1 Representations, Warranties and Covenants.

(a) Organization and Authority. Each Party represents and warrants that it (i) is duly organized, validly existing and, in the case of Cipher only, in good standing under the Laws of the jurisdiction of its organization, (ii) is qualified to do business in each other's jurisdiction in which the conduct of its business requires such qualification, (iii) is in compliance with all applicable Laws, relating to its business and assets, and (iv) is not in material default of its memorandum or articles of association, its certificate of incorporation or by-laws or all other constituent documents as the case may be, except in the case of (ii) and (iii) where such failure to qualify or be in compliance would not have a material adverse effect on the business and assets of such Party or the performance of this Agreement by such Party.

(b) Due Authorization and Enforceability. Each Party represents and warrants that (i) it has full authority to execute, deliver and perform its obligations under this Agreement, (ii) that this Agreement has been duly executed and delivered by such Party, and constitutes the legal, valid and binding obligations of such Party and is enforceable against such Party in accordance with its terms, and (iii) that the execution, delivery and performance of this Agreement will not violate, be inconsistent with or result in a default under or creation of lien or encumbrance under (except as specifically contemplated by this Agreement) (A) the memorandum or articles of association, certificate of incorporation or by-laws or other constituent documents, as the case may be, of any Party and/or its Affiliates, (B) any material agreement, contract, license understanding or instrument binding upon or affecting such Party or its properties or assets, whether express, implied, written or oral, or (C) any applicable Laws affecting either Party or its properties or assets, except where such violation would not have a material adverse effect on the business and assets of such Party.

(c) Import and Product Handling. Each Party covenants that it will and will cause its Affiliates and agents and, in the case of Distributor, its SubDistributors and, in the case of Can-Fite, its Approved Manufacturer(s) and, if applicable, Contract Finisher(s) to, comply with all applicable Laws relating to the importation, warehousing, storage, Manufacturing, Marketing, Packaging and Testing of Supplied Product applicable to such Laws and will ensure that all required Approvals are in effect and will maintain such Approvals in good standing.

(d) Rights to Grant. Can-Fite represents and warrants that it has the sole, exclusive and unencumbered right to grant the rights (including any license) herein granted to Distributor, and that neither Can-Fite, nor any other Person, has granted any option, license, right or interest in or to the Product to any Third Party which could conflict with the rights granted by it under this Agreement in the Territory.

(e) Trademarks. Can-Fite represents and warrants that, to its knowledge, it has all rights to the Can-Fite Trademarks and that such trademarks are valid. Distributor represents and warrants that, to its knowledge, it has all rights to the Trademarks and such trademarks are valid.

(f) Intellectual Property. Can-Fite represents, warrants and covenants that it owns or has the exclusive license to all intellectual property (including all Intellectual Property), assets, licenses and approvals necessary to make, have made, use, sell, offer for sale and import the Products for use in the Field on an exclusive basis and will possess all such rights during the Term as may be necessary to promote, market, distribute and sell the Product for use in the Field in the Territory itself and/or through Distributor or its Affiliates as contemplated by this Agreement. Can-Fite further represents, warrants and covenants that it has the right and ability to initiate patent litigation against Third Parties based upon an infringement of the Product Patents. Can-Fite represents and warrants that there is no other intellectual property (including, without limitation, any license to same) required for Can-Fite to Market, Manufacture or have Manufactured, Package or have Packaged, or Test or have Tested Product, or to grant Distributor the rights provided in this Agreement.

(g) No Claims. Can-Fite represents, warrants and covenants that there are no proceedings currently pending or, to the knowledge of Can-Fite, threatened against, Can-Fite or any of its Affiliates, relating to or otherwise arising from (i) Product Liability Claims or claims for death or bodily injury relating to any Product, or (ii) infringement, misappropriation or other conflict with any intellectual property or other rights of any Person relating to any Product or any Can-Fite Trademarks, or (iii) the promotion, marketing, manufacture, distribution or sale of any Products.

(h) No Infringement. Can-Fite represents and warrants that (i) to its knowledge, the Product does not and will not infringe the intellectual property rights of any Person; (ii) to its knowledge, Distributor's Marketing, sale and distribution of the Product as contemplated by this Agreement shall not infringe or otherwise violate the intellectual property rights of any person; and (iii) to its knowledge, the Manufacture and packaging of Product by an Approved Supplier including Distributor will not infringe the intellectual property rights of any Person.

11.2 Quality Assurance Representations, Warranties and Covenants.

(a) Can-Fite, in its own name and on behalf of any of its Approved Manufacturers, Contract Finishers and Affiliates engaged in the performance of the actions contemplated hereby, including the Manufacture, sale and delivery of Supplied Product hereunder, hereby represents, warrants and covenants to Distributor that all Supplied Product that Can-Fite or any of Can-Fite's Approved Manufacturers or Affiliates Manufactures, supplies and delivers under and pursuant to this Agreement will:

(i) conform to the Specifications at time of shipment to Distributor;

(ii) be free and clear from all liens, encumbrances and defects of title, other than those that arise directly as a result of actions taken by Distributor; and

(iii) comply in all material respects with the requirements under the GMP standards, the Regulatory Approvals and the Other Approvals, as applicable, the Act and any other applicable Law in the Territory, and will not, at the time of such delivery be adulterated or misbranded within the meaning of the Act.

(b) Can-Fite shall furnish to Distributor a certificate of analysis for each lot of the Supplied Product shipped to Distributor, and a certificate that such lot meets the quality control standards set forth in the relevant approved application for Regulatory Approval all well as the annual certificate of compliance.

(c) Distributor shall be responsible for storing Supplied Product under appropriate conditions as specified in labeling and for distribution in full compliance with the applicable GMP standards, the Regulatory Approvals, the Other Approvals, the Act and the applicable Law. Distributor shall have received and shall be in current compliance with all Approvals of any Authority as may be required to Market Supplied Product pursuant to this Agreement.

(d) None of Distributor or Distributor's Affiliates or SubDistributors shall, in bad faith, disrupt or cause the disruption of the supply of Supplied Product into the marketplace in the Territory.

(e) Can-Fite or its Approved Manufacturer(s) shall have received, and shall at all times during the Term, be in current compliance with, all Approvals of any Regulatory Authority as may be required to Manufacture and/or to supply the Supplied Product pursuant to this Agreement, and, as of the Effective Date, Can-Fite or, to its knowledge, any Approved Manufacturer has not received any warning letters or similar regulatory letters from any Regulatory Authority within the last three (3) years with respect to the Product which Can-Fite has not disclosed to Distributor or which prevents the Manufacture and supply of the Product.

(f) Can-Fite shall ensure that each lot of the Supplied Product shipped to Distributor has a shelf-life and expiration date of at least thirty-six (36) months at the date of shipment.

(g) Each Party represents and warrants to the other Party that it has not engaged in any conduct or activity which could justify an FDA debarment action, and no debarment proceedings are currently underway or, to its knowledge, contemplated against it or any of its employees and, to its knowledge, neither its Approved Manufacturer or any of its Contract Finishers has engaged in conduct that would justify an FDA debarment action and no proceedings are currently underway or contemplated against any of its Approved Manufacturers or Contract Finishers or any of their employees.

11.3 Distributor's Compliance with Laws.

Without limiting anything herein, Distributor shall comply with all applicable Laws in performing this Agreement, including all Marketing, promotional or advertising activities conducted by its Afiliates, or SubDistributors or its or their agents.

11.4 Limitation of Liability.

EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY TO THE OTHER PARTY OF ANY KIND, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

NOTWITHSTANDING ANYTHING TO THE CONTRARY CONTAINED IN THIS AGREEMENT, EXCEPT WITH RESPECT TO CONFIDENTIALITY AND INDEMNIFICATION OBLIGATIONS AS SET FORTH IN THIS AGREEMENT, IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER FOR ANY INCIDENTAL, CONSEQUENTIAL, SPECIAL, PUNITIVE, INDIRECT DAMAGES, LOSS OF PROFIT, LOSS OF REVENUE, LOSS OF USE EVEN IF INFORMED OF POSSIBILITIES OF SUCH DAMAGES OR LOSSES.

12. MISCELLANEOUS

12.1 Governing Law.

This Agreement shall be governed by laws of New York, excluding its choice of law provisions. The Parties hereby agree to exclude the application of the International Sale of Goods Act.

12.2 Dispute Resolution.

The Parties recognize that any dispute, controversy or claim arising under or relating to this Agreement, (collectively, a "**Dispute**") may from time to time arise during the Term of this Agreement including in relation to the selection and appointment of the Third Party Laboratory and Auditor. It is the objective of the Parties to establish procedures to facilitate the resolution of disputes arising under this Agreement in an expedient manner by mutual cooperation and without resort to litigation. To accomplish this objective, the Parties agree to follow the procedures set forth in this Section 12.2 if and when a dispute arises under this Agreement. Each Party shall designate an individual (the "**Responsible Person**") to whom disputes shall be initially referred. Such Responsible Person shall be (i) in the case of Can-Fite, a person having managerial responsibility in the functional area of dispute and (ii) in the case of the Distributor, a person having managerial responsibility in the functional area of dispute. Disputes under this Agreement between the Parties shall be submitted to the other Party's Responsible Person. The Responsible Persons will meet and hear the disputed matter in as timely a manner as possible. If the Responsible Persons are unable to reach a decision within ten (10) days, such matter shall be referred for resolution to the Chief Executive Officer of Can-Fite and the Chief Executive Officer of Distributor (or such other officer exercising the duties of such office). Such submission shall be made with each Party submitting a statement as to the disputed matter and the Responsible Persons providing a joint statement as to which matters they were unable to agree upon. In the event that a dispute is not resolved by the foregoing procedures within thirty (30) days of first being submitted by a Party, the matter shall be finally settled exclusively by arbitration under the International Arbitration Rules of the American Arbitration Association (the "**Rules**"), provided however that nothing herein shall prevent or prohibit any Party from seeking injunctive relief or non-monetary equitable relief as permitted in any court within appropriate jurisdiction. Either Party may, by written notice to the other, have a Dispute referred to arbitration. Unless otherwise agreed in writing, any arbitration shall be conducted in the English language and shall be held in New York City, New York, and heard by a panel of three (3) arbitrators. Each party shall nominate one arbitrator. The third arbitrator, who will be chairman of the arbitral tribunal, shall be appointed in accordance with the Rules. The decision and award of the arbitral tribunal shall be final and binding and may be entered in any court of competent jurisdiction, for which purpose, and for all other purposes under this Agreement, each party hereto submits to the exclusive jurisdiction and venue of the U.S. District Court for the Southern District of New York, or in the absence of jurisdiction of such court to the Supreme Court of New York County. The costs of any such arbitration shall be allocated as follows: (i) if the arbitrators rule in favor of one Party on all disputed issues in the arbitration, the losing Party shall pay one hundred percent (100%) of such out-of-pocket fees and expenses; and (ii) if the arbitrators rule in favor of one Party on some issues and the other Party on other issues, the arbitrators shall issue with the ruling a written determination as to how such fees and expenses shall be allocated between the Parties. At Distributor's request (but not absent such request) (i) the arbitrators may offset any amounts owed to Distributor against amounts owed by Distributor to Can-Fite, or may reduce the royalty rate on Net Sales or share of Net Profits so that Distributor may recoup amounts through the reduced royalty rate. At Can-Fite's request (but not absent such request) (i) the arbitrators may offset any amounts owed to Can-Fite against amounts owed by Can-Fite to Distributor or may increase the royalty rate on Net Sales or share of Net Profits so that Can-Fite may recoup amounts through the increased royalty rate. In no event may the arbitrators terminate this Agreement other than as provided in Section 9.2 or otherwise award punitive, special or consequential damages. The arbitrators shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the arbitration, with the Party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses. Each Party is required to continue to perform its obligations under this Agreement pending final resolution of the Dispute; provided that Can-Fite is only required to continue to supply Distributor with Supplied Product and replace rejected Supplied Product if Distributor makes payment for Supplied Product except as expressly provided for in this Agreement, including Sections 6.5 and 6.6 hereof. In no event will a demand for arbitration hereunder be made after the date when institution of a legal or equitable proceeding based upon such Dispute would otherwise be barred by the applicable statute of limitations. If a Dispute relating to payments is resolved by agreement of the Parties or by arbitration, and if the amount is not paid within ten (10) days of the Dispute resolution, the party entitled to payment (the "**Prevailing Party**") may setoff some or all of such amount against amounts it owes the other Party and in the case Distributor is the Prevailing Party it may in addition setoff the amount against future payments.

12.3 Entire Agreement; Amendments.

This Agreement, including the Schedules hereto, sets forth the entire terms of the supply and distribution arrangement between the Parties hereto and, except as otherwise set forth herein, supersedes and terminates all prior agreements and understandings between the Parties. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

12.4 Tax Withholding.

Can-Fite shall be liable for all income and other taxes (including interest) ("**Taxes**") imposed upon any payments made by Distributor to Can-Fite under this Agreement. If applicable laws, rules or regulations require the withholding of Taxes, Distributor shall make such withholding payments and shall subtract the amount thereof from payments under this Agreement; provided that the Parties shall use all reasonable and legal efforts to minimize tax withholding on payments made to the other Party hereunder. Distributor shall submit to Can-Fite appropriate proof of payment of the withheld Taxes as well as the official receipts within a reasonable period of time not to exceed sixty (60) days following the date of the Tax payment. Distributor shall provide Can-Fite reasonable assistance, which shall include the provision of such documentation as may be required by the tax authority, in order to allow Can-Fite to obtain the benefit of any present or future treaty against double taxation which may apply to such payments or to claim an exemption from or obtain a repayment or a reduction of such tax.

12.5 Notices.

When a Party is required or permitted to give notice under this Agreement, the notice shall be in writing, shall specifically refer to this Agreement and shall be deemed to have been sufficiently given and received for all purposes within (i) two (2) days if the Party sent the notice by internationally recognized express delivery service, (ii) one (1) day if the Party sent the notice by email, with acknowledgement of receipt and a prompt follow-up copy sent by an internationally recognized express delivery service, or (iii) immediately if the Party personally delivered the notice. Unless otherwise specified in writing, the mailing addresses of the Parties shall be as set forth below.

For Can-Fite:

Can-Fite Pharmaceuticals Inc.
10 Bareket Street
Kiryat Matalon
P.O. Box 7537
Petah-Tikva 49170
Israel

Email: pnina@canfite.co.il
Attention: Pnina Fishman

With a copy (which shall not constitute notice) sent simultaneously to:

Sichenzia Ross Friedman Ference LLP
61 Broadway, 32nd Floor
New York, NY 10006

Email: gsichenzia@srff.com
Attention: Gregory Sichenzia

For Distributor:

Cipher Pharmaceuticals Inc.
Tomken Road, Unit 16
Mississauga Ontario L4W 4P1

Email: sobrien@cipherpharma.com
Attention: Shawn Patrick O'Brien

With a copy (which shall not constitute notice) sent simultaneously to:

Torys LLP
Suite 3000, P.O. Box 270 79
Wellington Street West TD Centre
Toronto, ON M5K 1N2

E-mail: creicin@torys.com
Attention: Cheryl V. Reicin

Copies (other than to outside counsel) are an integral part of notice. ***Notices of termination may only be sent by internationally recognized express delivery service or by personal delivery.***

12.6 Assignment.

Neither Party shall assign or otherwise transfer this Agreement or any interest herein or right or obligation hereunder without the prior written consent of the other Party not to be unreasonably withheld, and any such purported assignment, transfer or attempt to assign or transfer any interest herein or right hereunder shall be void and of no effect; *provided, however*, that a Party may assign its rights and obligations hereunder to an Affiliate or to a transferee or acquirer of, or successor to, its assets or securities in the event of a merger, sale of stock, sale of assets or other transaction without the prior consent of the other Party; *provided, further* that (i) in the case of an assignment to an Affiliate, the assigning Party shall remain responsible for all of its obligations and agreements set forth herein, notwithstanding such assignment, and (ii) in the case of a merger, sale of stock, sale of assets, assignments or other transaction, such transferee or successor shall assume in writing the obligations of the party to which it is the transferee or successor, including, without limitation, those set forth in Sections 2.2, 2.3 and 2.4 hereof; and (iii) either Party may have its Affiliates perform its obligations hereunder; provided that the delegating Party shall remain responsible for all of its obligations and agreements set forth herein, notwithstanding such delegation. Notwithstanding the foregoing, the licensor of intellectual property to Distributor under this Agreement shall be an entity of a jurisdiction having legal protections in the event of a bankruptcy or reorganization filing of the licensor, which in the reasonable opinion of Distributor, are comparable or at least as favorable to a licensee as those provided under Israeli law, as in effect as of the Effective Date.

12.7 Public Announcements.

Neither Party shall make any publicity releases, interviews or other dissemination of Confidential Information concerning Supplied Product (the purpose of which is not advertisement or promotion), this Agreement or its terms, or either Party's performance hereunder, to communication media, financial analysts or others without the prior written approval of the other Party, which approval shall not be unreasonably withheld, conditioned or delayed. Either Party may, upon written notice to the other, make any disclosure in filings with Authorities as required by Law or applicable court or other order; *provided, however*, that the other Party shall have not less than three (3) Business Days to review and comment on such disclosures and filings unless a shorter period is necessitated by securities laws.

12.8 Severance.

If any Official Body or Regulatory Authority having jurisdiction over either Can-Fite or Distributor declares any Article or part thereof invalid or any such Official Body or Regulatory Authority deems any Article or part thereof to be contrary to any Laws, then such Article or part thereof shall be deemed stricken from this Agreement in that jurisdiction. To the extent possible the Parties shall revise such invalidated Article or part thereof in a manner that will render such provision valid without impairing the Parties' original intent.

12.9 Non-Waiver.

The failure of a Party in any one or more instances to insist upon strict performance of any of the terms and conditions of this Agreement shall not be construed as a waiver or relinquishment, to any extent, of the right to assert or rely upon any such terms or conditions on any future occasion. Except as otherwise specified, all rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be a limitation of any other remedy, right, undertaking, obligation or agreement.

12.10 Further Assurances.

Each Party hereto agrees to execute such further documents and take such further steps as the other Party reasonably determines may be necessary or desirable to effectuate the purposes of this Agreement.

12.11 Force Majeure.

No Party shall be in breach of this Agreement, or liable to the other Party, for any delay or failure of performance to the extent such delay or failure is caused by Force Majeure, provided that the Party claiming Force Majeure gives prompt written notice to the other Party of the occurrence of an event of Force Majeure and uses its commercially reasonable efforts to overcome the same. In the event of Force Majeure, the Parties agree to discuss the circumstances and effects thereof, including the effects on Distributor's obligations under this Agreement, and appropriate mechanisms to address such circumstances and effects.

12.12 Anti-Corruption.

Can-Fite and Distributor each agrees that it shall comply with the requirements of applicable obligations imposed by the anti-bribery laws and foreign corrupt practices laws of all applicable jurisdictions in which the services contemplated hereunder are rendered, or obligations contemplated hereunder are carried out, and the laws of any other jurisdiction in which Can-Fite, Distributor and any of their personnel, agents or representatives conduct business in relation to dealing with payments to governments or related persons or officials, or a company, for the purpose of obtaining or retaining business for or with, or directing business to, any person. For greater certainty, the foregoing laws shall include, among others, the *Foreign Corrupt Practices Act of the United States of America*, the *Lobbyists Registration Act* (Canada), the *Corruption of Foreign Public Officials Act* (Canada), and the *Criminal Code* of Canada and any corresponding Israeli laws.

12.13 Disclaimer of Agency.

This Agreement shall not constitute either Party the legal representative or agent of the other Party, nor shall either Party have the right or authority to assume, create, or incur any Third Party liability or obligation of any kind, express or implied, against or in the name of or on behalf of another except as expressly set forth in this Agreement. None of the Distributor, its directors, officers, agents or employees shall be considered employees agents or legal representatives of Can-Fite for any purpose. None of Can-Fite, its directors, officers, agents or employees shall be considered employees agents or legal representatives of Distributor for any purpose.

12.14 Construction.

The language in all parts of this Agreement shall be construed, in all cases, according to its fair meaning. The Parties acknowledge that each Party and its counsel have reviewed and revised this Agreement and that any rule of construction to the effect that any ambiguities are to be resolved against the drafting Party shall not be employed in the interpretation of this Agreement. The words “hereof,” “herein,” “hereto” and “hereunder” and words of similar import, when used in this Agreement, shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The terms defined in the singular shall have a comparable meaning when used in the plural, and vice versa. The terms “dollars” and “$” shall mean Canadian dollars. Whenever used herein, the words “include,” “includes” and “including” shall mean “include, without limitation,” “includes, without limitation” and “including, without limitation” respectively, whether or not the term “without limitation” appears after the words “include,” “includes” or “including”. The masculine, feminine or neuter gender and the singular or plural number shall each be deemed to include the others whenever the context so indicates.

12.15 Counterparts.

This Agreement shall become binding when any one or more counterparts hereof, individually or taken together, shall bear the signatures of each of the Parties hereto. This Agreement may be executed in any number of counterparts, including by email or facsimile, each of which shall be deemed an original as against the Party whose signature appears thereon, but all which taken together shall constitute but one and the same document.

12.16 Consents in Writing.

Any consents required hereunder from a Party must be in writing.

Signature Page Follows

IN WITNESS WHEREOF, the Parties hereto have duly executed this Agreement as of the date first written above.

CAN-FITE BIOPHARMA LTD.

By: /s/ Pnina Fishman
Name: Dr. Pnina Fishman
Title: Chief Executive Officer

CIPHER PHARMACEUTICALS INC.

By: /s/ Shawn O'Brien
Name:
Title:

[SIGNATURE PAGE TO DISTRIBUTION AND SUPPLY AGREEMENT]

SCHEDULE A
CAN-FITE TRADEMARKS AND PATENTS

Trademarks

At the Effective Date Can-Fite makes use of its internal code name CF101 to designate the Product.

Can-Fite has not adopted any trademark for the Product.

Patents

At the Effective Date the Company has the following Canadian patents and patent applications relating to the Product:

Issued patent No. 2,384,111

Issued patent No. 2,434,906

Pending patent application No. 2,586,773

Issued patent No. 2,662,879

Pending patent application No. 2,761,499

Pending patent application No. 2,790,869

Pending patent application No. 2,880,753

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(71) Applicant *(for all designated States except US)*: **CAN-FITE BIOPHARMA LTD.** [IL/IL]; 10 Bareket Street, P.O. Box 7537, 49170 Petach Tikva (IL).

(72) Inventors; and

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(54) Title: PROCESS FOR THE SYNTHESIS OF IB-MECA

(57) Abstract: The present disclosure provides a method for the synthesis of IB-MECA. More specifically, the present disclosure provides a simple and high yield method for Good Manufacturing Production (GMP) of IB-MECA. The method involves the reaction of 6-halopurine-9-riboside with a diol protecting reagent; oxidation of the primary alcohol in the diol protected 6-halopurine; reaction of the diol protected 6-halopurine with a nucleophile (e.g. methylamine); substitution of the halogen group with iodobenzylamine and removal of the diol protecting group.

WO 2008/111082 A1

PROCESS FOR THE SYNTHESIS OF IB-MECA

FIELD OF THE INVENTION

This invention is in the field of chemistry and in particular relates to the synthesis of an A_3 adenosine receptor agonist.

BACKGROUND OF THE INVENTION

Adenosine is a ubiquitous purine nucleoside which is secreted extra-cellularly by metabolically active and stressed cells. Adenosine is an important regulatory molecule through its binding to at least 4 G-protein-associated cell surface receptors, currently classified A_1, A_{2a}, A_{2b} and A_3 [Linden B. *TiPS* 15: 298-306 (1994); Poulsen S, *Bioorg Med Chem* 6: 619-41 (1998)].

Almost all human tissues express adenosine receptors of 1 or more classes, and this includes, in high density, various tumor cells [Merighi S, et al. *Br. J. Pharmacol.* 134: 1215–1226 (2001)]. A_1 and A_3 receptor activation causes G-protein signal transduction leading to reduced activity of kinases PKB/Akt and PKA, and decreased formation of cAMP; this inhibits cell growth [Fishman P, et al. *Oncogene* 21: 4060–4064 (2002)].

1-deoxy-1-(6-{[(3-iodophenyl)methyl]amino}9H-purine-9-yl)-*N*-methyl-β-d-ribofuranuronamide (methyl 1-[N6-(3-iodobenzyl)-adenin-9-yl]-β-D-ibofuronamide, IB-MECA; MW=510.29 Da) is an orally active adenosine receptor agonist with specific, submicromolar potency at the A_3 receptor (K_i = 0.47M).

In vivo, orally administered IB-MECA inhibits the development of tumors in syngeneic (melanoma, colon carcinoma) and xenograft (colon and prostate carcinoma) mouse models [Fishman P. et al. *Anticancer Res.* 23(3A): 2077-2083 (2003)].

It has also been found that giving IB-MECA orally to mice stimulates the production of neutrophils via an increase in granulocyte colony stimulating factor (G-CSF) and, correspondingly, IB-MECA protects against cytotoxic-induced

myelo-toxicity [Bar-Yehuda S, et al. *Exp. Hematol.* 30: 1390–139 (2002)]. Oral IB-MECA also inhibits progression of colon carcinoma in nude mice, and stimulates neutrophil recovery after cytotoxic drug therapy in this strain.

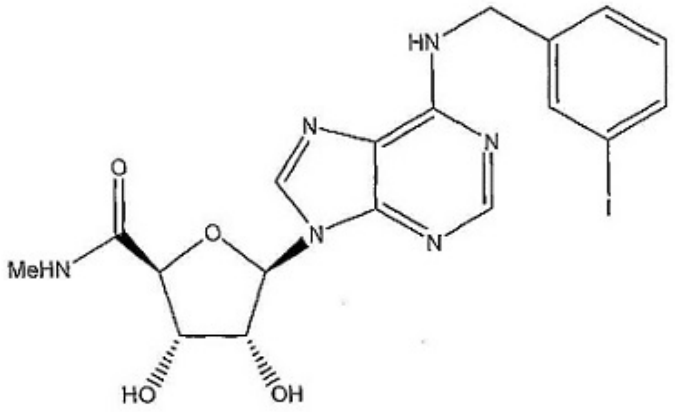
Considerable evidence has been accumulated indicating that adenosine through its receptors play also an important role in limiting inflammation. Adenosine's anti-inflammatory effects are manifested by inhibition of TNF-α, interleukin-1 and interleukin-6 production. The involvement of adenosine in mediating the effect of several anti-inflammatory drugs such as aspirin, methotrexate and sulfasalazin has been described, supporting the role of adenosine in the regulation of the inflammatory process. Recent studies suggested that the highly selective A_3 adenosine receptor (A_3AR) agonist IB-MECA inhibited the production of TNF-α and MIP-1α *in vitro* while preventing the development of collagen and adjuvant induced arthritis (AIA) in experimental animal models (WO2004/045627). In addition, it has been shown that A_3AR is highly expressed in synovial and peripheral blood mononuclear cells (PBMNC) of AIA rats and its level down regulates upon IB-MECA treatment (WO 2004/038419).

The chemical synthesis of adenosine A_3 receptor selective agonists, particularly adenine compounds, among others, the IB-MECA, was first described by Jacobson K. et al. in U.S. Pat. No. 5,773,423.

US Patent application publication No. 2006/0014944 describes a method for the synthesis of nucleotides.

SUMMARY OF THE INVENTION

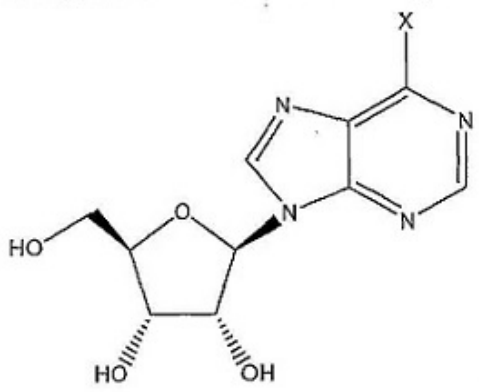
According to the first of its aspects, the invention provides a method for the chemical synthesis of IB-MECA, having the following formula (I):



(I)

The method in accordance with the invention comprises:

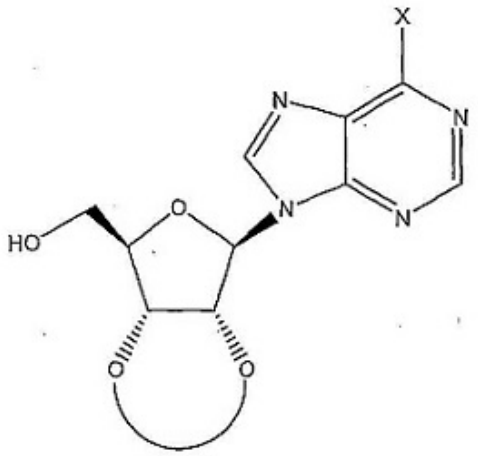
(i) reacting 6-halopurine-9-riboside of the following formula (II):



(II)

wherein X is a halogen selected from Cl, I or Br;

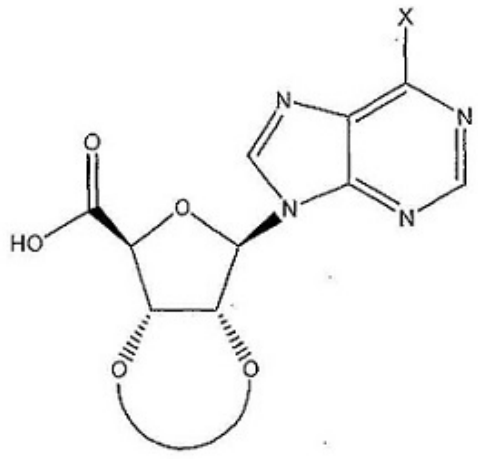
with a diol protecting reagent to obtain a diol protected 6-halopurine of the following formula (III):



(III)

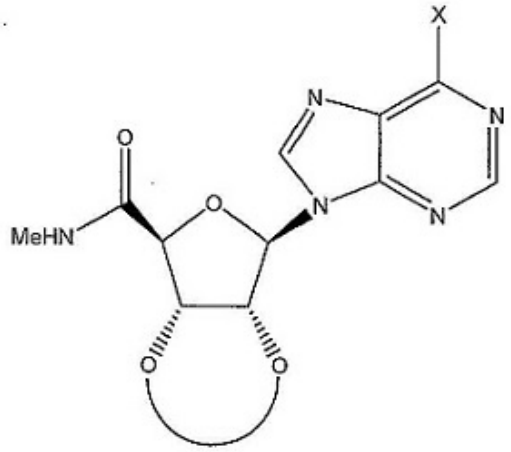
wherein said diol protecting reagent comprises a straight or branched C_1-C_6 alkyl group;

(ii) oxidizing the primary alcohol in said diol protected 6-halopurine of formula (III) to a respective carboxylic acid derivative of formula (IV):



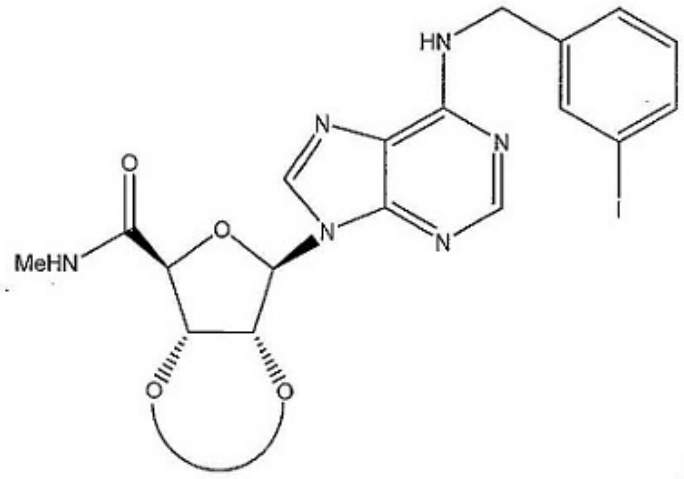
(IV)

(iii) reacting the carboxylic acid group of the derivative of formula (IV), with a methylamine to obtain the respective methylamide derivative of the diol protected 6-halopurine (III), the methylamide derivative having the formula (V):



(V)

(iv) substituting the halogen group of said methylamide derivative (V) with 3-iodobenzylamine to form a diol protected IB-MECA having the formula (VI);



(VI)

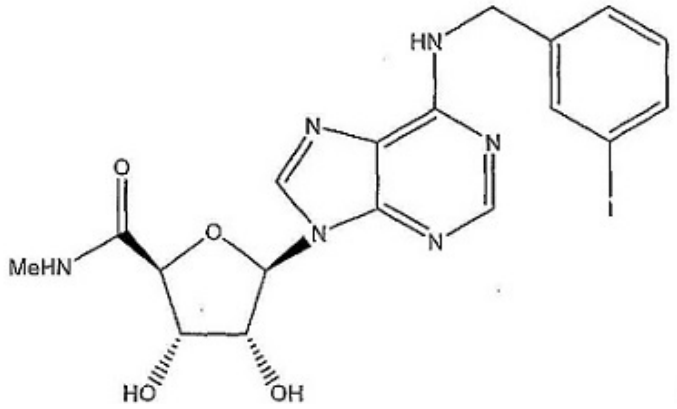
(v) removing the diol protection to obtain said IB-MECA of formula (I).

The invention also provides chemically synthesized IB-MECA whenever obtained by the method of the invention as well as pharmaceutical compositions comprising the said chemically synthesized IB-MECA.

DETAILED DESCRIPTION OF SOME EXEMPLARY EMBODIMENTS

The present invention is based on the development of an efficient method for the synthesis of IB-MECA, and the finding that this method is also suitable for current good manufacturing production (cGMP) of IB-MECA. It is noted that IB-MECA is referred to at times by the term CF101.

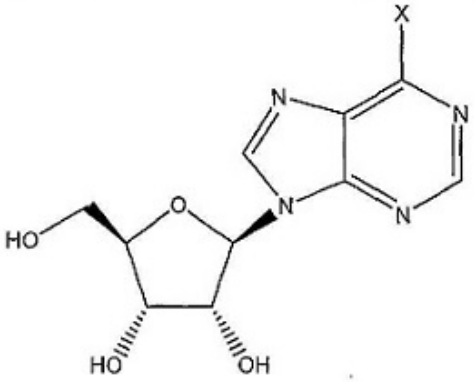
Thus, there is disclosed herein a method for the chemical synthesis of IB-MECA, having the following formula (I):



(I)

the method comprising :

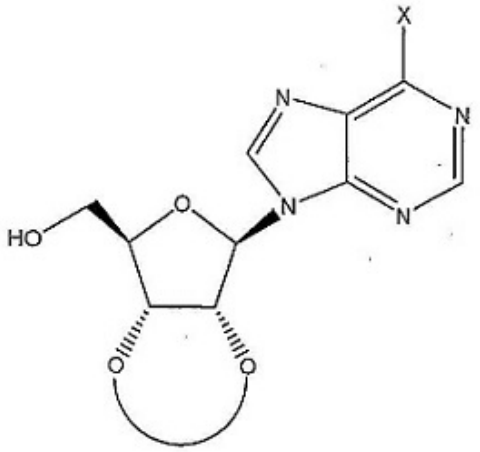
(i) reacting 6-halopurine-9-riboside of the following formula (II):



(II)

wherein X is a halogen selected from Cl, I or Br;

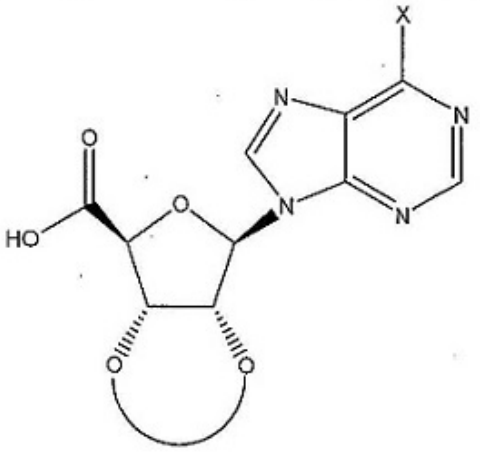
with a diol protecting reagent to obtain a diol protected 6-halopurine of the following formula (III):



(III)

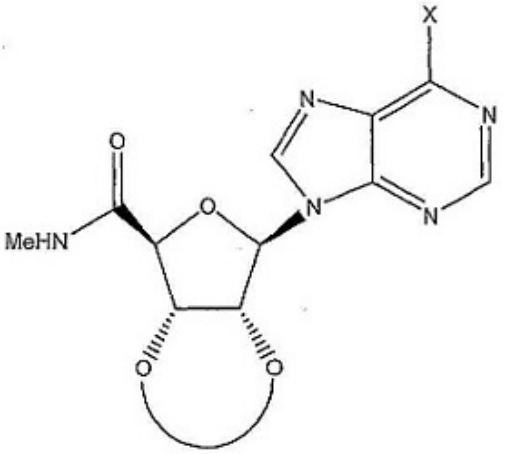
wherein said diol protecting reagent comprises a straight or branched C_1-C_6 alkyl group;

(ii) oxidizing the primary alcohol in said diol protected 6-halopurine of formula (III) to a respective carboxyl derivative of formula (IV):



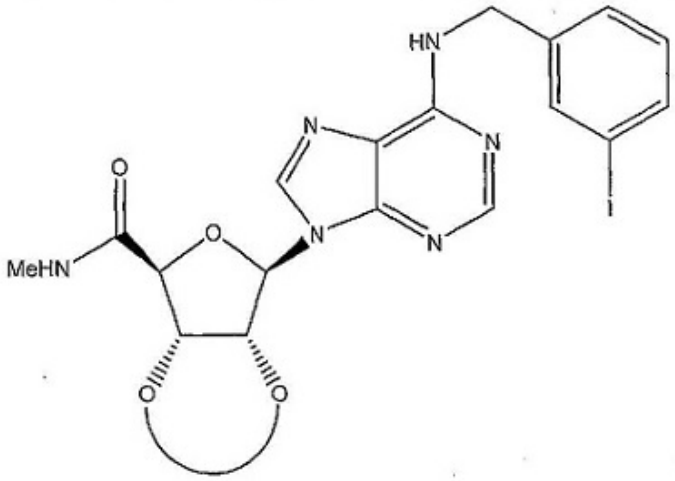
(IV)

(iii) reacting the carboxylic acid group of the derivative of formula (IV) with a methylamine to obtain the respective methylamide derivative of the diol protected 6-halopurine (III), the methylamide derivative having the formula (V):



(V)

(iv) substituting the halogen group of methylamide derivative (V) with 3-iodobenzylamine to form a diol protected IB-MECA having the formula (VI); and



(VI)

(v) removing diol protection to obtain said IB-MECA of formula (I).

In the present disclosure, the term "*protecting reagent*" is used to denote any chemical moiety which is introduced into a molecule by chemical modification of a functional group in order to obtain chemoselectivity in a subsequent chemical reaction. A variety of protecting reagents are known to those versed in the art of organic chemistry. As used herein, the protecting reagent reacts with a functional group(s) a substrate molecule to form a protected substrate. This protected substrate is stable to reaction conditions to which the protected substrate will be subjected after which it is removable

from a protected substrate to liberate the functional group(s) under conditions that are compatible with other functionality present in the substrate. The hydroxyl groups of 1,2-diols may be individually protected or may be jointly protected with a cyclic diol protecting group. Examples of suitable hydroxyl protecting groups and diol protecting groups may be found in T.W. Greene et al. *"Protective Groups in Organic Synthesis"*, 3rd Ed., John Wiley and c Sons Inc., NY (1999), which is incorporated herein by reference.

In accordance with the present disclosure the protecting reagent comprises a C_1-C_6 alkyl moiety. In one embodiment disclosed herein, the protection of the diol funtional group is achieved when reacting a molecule comprising said diol group with a protecting reagent, for example, and without being limited thereto, with C_3-C_6 dialkyloxyalkane, thereby forming a protective cyclic acetal moiety on a substrate molecule, readily removed with appropriate reaction conditions known in the art. Preferably, the dialkyloxyalkane is dimethoxypropane.

In another embodiment, the diol protection is achieved in the presence of a strong acid and a polar organic solvent. The strong acid may be selected from, without being limited thereto, p-TsOH, methane sulfonic acid, benzene sulfonic acid, formic acid, hydrochloric acid, sulfuric acid. The polar organic solvent may be, in accordance with another embodiment, a water-miscible solvent. A non-limiting example for the polar organic solvent is acetone. Others may include ethyl acetate, methylethyl ketone, chloroform, ethanol, methanol and others.

The term *"functional group"* is used herein to denote atoms or groups of atoms within molecules that are responsible for the physical and chemical characteristic of the molecule with respect to its physical properties and the possible reactions it may undergo with other reagents. A variety of functional groups are known with respect to chemical compounds. In accordance with one embodiment, the functional group is a diol group present on the furan ring. In an embodiment disclosed herein, the *"diol"* functional group refers to the two hydroxyl groups (-OH groups) attached to adjacent carbon atoms.

The term *"oxidizing agent"* as used herein refers to any substance in a reaction that gains electrons and whose oxidation number is decreased. In a typical reaction the

oxidizing agent readily transfers oxygen atoms to a reactant, for example, the diol protected 6-halopurine of formula (III), thereby increasing its oxygen atoms content.

In the context of the present disclosure the terms "*substitution*" and "*substituting*", or "*replacing*" which may be used intechangibly, denote any replacement of an atom, a moiety, a functional group, or a substituent in a reactant molecule, by, independently, another atom, a moiety, a functional group, or a substituent in a reactant molecule.

In the context of the present disclosure the term "*nucleophilic substitution*" relates to a reaction in which an electron-rich reagent, having either a pair of unshared electrons or a negatively charged moiety, referred to as the "*nucleophileic reagent*" attacks a positive or partially positive moiety of a substrate molecule (for example the carboxylic carbon of an acyl chloride) and replaces a group or atom (also called a "leaving group", for example the chloride anion of the attached acyl chloride substrate).

In a further embodiment disclosed herein the oxidation of the primary alcohol in the diol protected 6-halopurine of formula (III) to the corresponding carboxylic acid derivative is executed in the presence of a catalytic amount of an oxidizing agent.

A non-limiting list of oxidizing agents which may be suitable for the oxidation of primary alcohols to the corresponding carboxylic acids, comprises ruthenium metal (Ru), ruthenium chloride, chromium trioxide, sodium periodate, potassium dichromate, potassium permanganate, silver oxide, nitric acid, platinum oxide/oxygen, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), sodium chlorite and any combination thereof. Preferably, said oxidation is executed in the presence of a catalytic amount of $RuCl_3$ and sodium periodate.

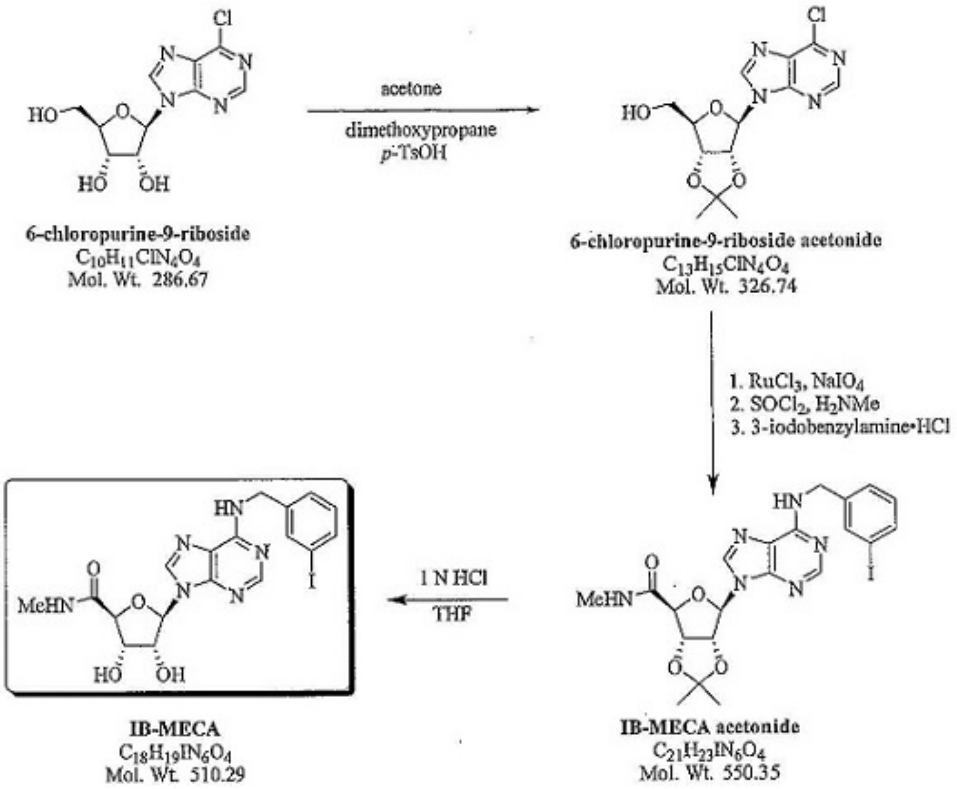
The conversion of carboxylic acid derivative of formula (IV) to the respective methylamide derivative of formula (V) is executed by nucleophilic substitution in the presence of an halogenating agent and thereafter introducing the selected nucleophilic reagent, e.g. methylamine.

The term "*halogenating agent*" as referred to in the present context of the disclosure, concerns an agent capable of replacing a group or moiety in a molecule with a

halogen atom. In the context of the present disclosure the halogenating agent replaces the hydroxyl group on the carboxylic acid moiety, thereby making it more prone to the nucleophilic substitution reaction with the methylamine nucleophile, since the group replaced would be a halogen anion, known to be a weak Lewis base, i.e. easily replaced by the nucleophile. Non-limiting examples of halogenating agents include thionyl chloride ($SOCl_2$), phosphorous pentachloride (PCl_5). Preferably, the halogenating agent is thionyl chloride.

Finally, the protecting group on the diol moiety of the furan ring is removed. Typically and without being bound by theory, the removal of protecting groups is a reductive cleavage reaction, preformed in the presence of strong acids. The removal of the diol protecting group may be performed in the presence of a strong acid and a polar non-protic solvent. In accordance with one embodiment, the strong acid is HCl and the solvent is tetrahydrofuran (THF). Other polar non-protic solvents known in the art may also be employed at this stage of reaction process, including but not limited to dimethyl sulfoxide (DMSO), dimethylformamide (DMF), dioxanes and hexamethylphosphorotriamide (HMPA).

In one embodiment, the method of producing IB-MECA is obtained in accordance with the following scheme:



6-chloropurine-9-riboside
$C_{10}H_{11}ClN_4O_4$
Mol. Wt. 286.67

6-chloropurine-9-riboside acetonide
$C_{13}H_{15}ClN_4O_4$
Mol. Wt. 326.74

IB-MECA
$C_{18}H_{19}IN_6O_4$
Mol. Wt. 510.29

IB-MECA acetonide
$C_{21}H_{23}IN_6O_4$
Mol. Wt. 550.35

One advantage of the method of the invention is that it is applicable also large scale production of IB-MECA.

In the context of the present disclosure, large scale production refers to tens of grams to kilogram quantities of material of final product. As shown in the specific examples, there is no need for interim purification procedures. As appreciated by those versed in the art, interim purification steps lead to lower yields of the final product and therefore are typically not suitable for large scale productions. The method of the invention was found to be suitable for small scale as well as large scale production of IB-MECA.

Further, it was established that the method of the invention is suitable for *Good Manufacturing Production* (GMP) of IB-MECA. It is well known that GMP denotes the set of regulations, codes, and guidelines for the manufacture of drug substances (also

known as active pharmaceutical ingredients (APIs)) and drug products (known as medicinal products in Europe), medical devices, *in vivo* and *in vitro* diagnostic products, and foods. In the United States, GMPs are referred to as "*cGMP*" or "*current Good Manufacturing Practices*". This term is recognized worldwide for the control and management of manufacturing and quality control testing of pharmaceutical products.

In another aspect of the present disclosure there is provided a chemically synthesized IB-MECA of formula (I), whenever obtained by any method of the invention.

In one further embodiment of the present disclosure there is provided a pharmaceutical composition comprising the chemically synthesized IB-MECA whenever obtained by the method of the invention.

The pharmaceutical composition of the invention may be used for the treatment or prevention of various diseases. The term "*treatment*" and the like are used herein to refer to obtaining a desired pharmacological and physiological effect. The effect may be prophylactic in terms of preventing or partially preventing a disease, symptom or condition thereof and/or may be therapeutic in terms of a partial or complete cure of a disease, condition, symptom or adverse effect attributed to the disease. The term "*treatment*" , as used herein, covers any treatment of a disease in a mammal, particularly a human, and includes: (a) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it, i e., causing the clinical symptoms of the disease not to develop in a subject that may be predisposed to the disease but does not yet experience or display symptoms of the disease; (b) inhibiting the disease, i.e. , arresting or reducing the development of the disease or its clinical symptoms; or (c) relieving the disease, i.e., causing regression of the disease and/or its symptoms or conditions.

A non-limiting list of diseases treatable by the composition of the invention comprise inflammation, as generally described in WO 2004/045627; WO 2005/063246; WO/2005/111053 and in WO 2006/059328; cancer, as generally described in WO2000/040251, and US provisional patent application No. 60/838,863; dry eye as generally described in PCT patent application No. IL2006/000130; WO2006/011130 and in US patent application No. 11/604,905; viral replication, as generally described in

WO02/055085; osteoarthritis as generally described in PCT application No. IL2006/001374; as well as accelerated bone resorption as generally described in WO 2006/048884; the content of all the above applications being incorporated herein by reference.

EXEMPLES

Materials

6-Chloropurine-9-ribose (obtained from Wilshire Technologies)

p-TsOH H_2O (obtained from Aldrich)

2,2-dimethoxypropane (obtained from Aldrich)

Ruthenium (III) chloride hydrate (obtained from Aldrich)

3-iodobenzylamine HCl (obtained from Apollo)

TBAI (obtained from Aldrich)

CH_3CN (obtained from Fisher)

H_2NCH_3 (obtained from Aldrich)

$SOCl_2$ (obtained from Aldrich)

$NaIO_4$ (obtained from Aldrich)

Methods

EXAMPLE 1: Synthesis of IB-MECA

1. Preparation of Acetonide (III)

1.1 The synthesis procedure

6-Chloropurine-9-ribose acetonide (III) was prepared from commercially available 6-chloropurine-9-ribose (II) by treatment with 2,2-dimethoxypropane in the presence of catalytic p-toluenesulfonic acid.

The conversion of the riboside (II) to the acetonide (III) required approximately 48 hours to reach completion at 20—25°C. The workup method used is *outlined* below and involved quenching with aqueous sodium hydroxide, concentration of the mixture to dryness followed by an extractive aqueous workup into methylene chloride. Acetonide (III) was then isolated by drying over magnesium sulfate, filtration to remove the drying

agent, solvent exchange into acetonitrile to precipitate the product, collection by filtration and drying *in vacuo*. A second crop of acetonide (III) was obtained by concentration of the mother liquors and isolation from slurry in acetonitrile. The combined (two crops) yield of acetonide (III) from 6-chloropurine-9-ribose (II) was 85.7%.

Following is an *Outline* of the synthetic step preformed for the preparation of acetonide (III) (all reagents, weight and volume equivalents are quoted with respect to the input of 6-chloro-9-riboside (II)):

- Riboside of formula II (1 wt equiv) was added to acetone (23 vol) and agitation of the reaction mixture was initiated.
- TsOH (0.05 equiv) and 2,2-dimethoxypropane (3.5 equiv) were then added to the reaction mixture.
- The reaction mixture was stirred at 20°C—25°C for 48—96 hours during which samples were taken for determining reaction completion by HPLC. Completion condition was determined when riboside (II) is not more than (NMT) 2%.
- The reaction was then quenched by the addition of 1N NaOH (0.052 equiv) and stirring for one hour.
- The resulting mixture was then dried using rotary evaporation at 30°C-40°C.
- The resulting residue was then partitioned between CH_2Cl_2 (10 vol) and water (10 vol), stirred for 15 minutes and allowed to settle.
- The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 3 vol).
- The organic extracts were combined and dried over $MgSO_4$ (2.5 wt equiv).
- The mixture of extracts were filtered through a diatomaceous earth pad and the cake was with CH_2Cl_2 (1.5 vol).
- The filtrate was concentrated to dryness by rotary evaporation at 30°C—40°C.
- The residue was slurred in CH_3CN (2 vol) at 55°C—65°C for one hour.

- The slurry was cooled to 0°C—10°C, then aged at 0°C—10°C for at least one hour.
- The product was then collected by filtration and washing the resulting cake with cold CH_3CN (0.5 vol).
- The product (the cake) was dried at 25°—35°C to give acetonide of formula III (first crop). The expected yield was 59—76%; purity was 96.6 to 99.5%.
- To increase yield, the mother liquor was recovered for second crop:
- The filtrate was concentrated from the second crop to dryness.
- The residue was slurred in CH_3CN (0.15 vol) at 55°C to 65°C for at least 30 minutes.
- The product was cooled to 0°C—10°C and aged at 0°C for at least one hour.
- The product (the cake) was collected by filtration and washed with cold CH_3CN (0.03 vol).
- The product was dried at 25°C—35°C to give acetonide of formula III (second crop). The expected yield was 9—14%; purity was 96.2 to 97.8%

Expected yield from two crops was 73—85%.

1.1 Optimization of the process for preparation of acetonide (III)

Riboside of formula II (30 g) was reacted with 2,2-dimethoxypropane, using the established conditions (Steps 1—3, in above *Outline*), to give acetonide (III) as a solution in acetone. The mixture was quenched with 1N aqueous sodium hydroxide solution (Step 4, in above *Outline*) and split into portions.

1.2 Isolation of acetonide (III) from Water

The acetone solution above was concentrated, by rotary evaporation under reduced pressure, to nine volumes then diluted with water (27 vol) and mechanically stirred for 20 minutes. The batch temperature increased from 23 to 28°C and some precipitation was observed. The mixture was cooled to 4°C and aged at 3—5°C for one hour. Precipitation of the material as a fine crystalline solid was observed. The precipitate

was collected by filtration, washed with water-acetone (2:1, 1.5 vol) and dried under vacuum (30 in. Hg) at ambient temperature to afford acetonide (III) as a pale yellow solid in 68% yield and 98.8% purity (AUC, HPLC).

In order to enhance the yield of acetonide (III), its isolation was preformed from a more concentrated acetone/water mixture. Therefore, the acetone solution was concentrated to nine volumes, as above, then diluted with water (9 vol) and stirred for 10 minutes The mixture was further concentrated to 12.5 volumes (the estimated acetone-water ratio was 2.6:1) and the product precipitated as a fine crystalline material. The mixture was cooled with stirring to 5°C, aged for 30 minutes then the product was collected by filtration, washed with water-acetone (2:1, 1.5 vol) and dried under vacuum at ambient temperature to afford acetonide (III) as a pale yellow solid in 80% yield and 99.3% purity (AUC, HPLC). Both the yield and purity of acetonide (III) were enhanced using this method.

1.3 Isolation of acetonide (III) from acetonitrile

The acetone solution was concentrated to six volumes, under reduced pressure, and the product precipitated from the quenched reaction mixture. Acetonitrile (15 vol) was required to solubilize the bulk of the solids. The mixture was clarified and the filtrate was concentrated by rotary evaporation under reduced pressure to three volumes. The resulting slurry was agitated at 60°C (bath temperature) for one hour, then cooled to 5°C and aged for one hour. The product was collected by filtration, washed with water-acetone (2:1, 1.5 vol) and dried under vacuum at ambient temperature to afford acetonide 2 as a pale yellow solid in 65% yield and 98.5% purity (AUC, HPLC).

It was clear from these experiments that acetonide (III) was relatively insoluble in both water and acetonitrile compared to acetone. The best results had been obtained by isolation of acetonide (III) from water/acetone. The reaction was repeated and acetonide (III) was prepared in 79% yield (27.1 g) and 99.54% purity (AUC, HPLC) from riboside (II) (30 g) using the modifications described above. The optimized conditions allowed the removal of the liquid-liquid extraction step, two evaporations to dryness and the need to

isolate a second crop of acetonide (III). The improved efficiency of the workup procedure has significantly reduced the cycle time for the isolation of acetonide (III).

2. *Process for the Preparation of Carboxylic Acid (IV)*

2.1 The synthesis procedure

Acetonide (III) was converted to carboxylic acid (IV) by oxidation using a ruthenium trichioride/sodium periodate system in aqueous acetonitrile. The reaction is exothermic, warming relatively rapidly from 5°C to 31°C upon addition of the sodium periodate.

Following is an *Outline* of the synthetic steps for the preparation of carboxylic acid (IV):

1. Acetonide of formula III (1 wt equiv) and acetonitrile (14.9 vol) were placed in a reactor.
2. In addition, to the reactor $RuCl_3$ (0.01 wt, 1.6 mol %) was added and then water (4 vol).
3. Then, tertabutylammonium iodide (TBAI) was added to the reactor (0.01 wt, 1 mol %).
4. The resulting mixture was Cooled to <5°C.
5. To the cooled reaction mixture $NaIO_4$ (1.5 wt, 2 equiv) was added, in a portion-wise manner, maintaining the mixture's temperature at <30°C.
6. The mixture was stirred at 15°C—30°C and monitored by TLC for reaction completion.
7. The reaction product was filtered to remove inorganics and the filtered cake was rinsed with acetonitrile (6 vol).
8. The filtrate was concentrated on a rotovap to dryness at 30°C—40°C (bath temperature). At this stage the product decolorized by evaporation of volatile RuO_4.
9. The residue was slurred in THF (1.67 vol) at 15°C—25°C and transferred from the rotovap bulb into a clean reactor.

10. THF (18.5 vol) was added into the clean reactor and stirred for 30 minutes.
11. The product of step 10 was then filtered through a DE pad and the cake was rinsed with THF (0.66 vol).
12. The filtrate was concentrated to dryness by rotary evaporation at 30°C—40 °C.
13. The residue was slurred in CH_3CN (2.33 vol) at 30—40°C until fully mobile.
14. The product of step 13 was then concentrated to dryness by rotary evaporation at 30°C—40 °C.
15. IPAc (Isopropyl acetate) (17.5 vol) was added in portions to a reactor via the rotovap bulb, and the reaction product was transfered to the reactor.
16. Water (5 vol) was also added to the reactor and the mixture in the reactor was stirred for two hours.
17. The phases were separated and the organic phase was washed with water (5 vol).
18. The aqueous phases were combined and back-extracted with IPAc (3 vol).
19. The organic phases were combined and dried over Na_2SO_4 (1.67 wt equiv) for one hour.
20. The product was filtered to remove the drying agent and the filtrate (cake) was rinsed with IPAc (2 vol).
21. The filtrate was then collected to dryness by rotary evaporation (30°C—40°C).
22. The residue was then dried in a vacuum oven at 30°C—40°C to constant weight. The solid was ground and drying continued until constant weight was achieved. Expected yield was 85%, expected purity was 92—93% (HPLC).

2.1 Optimization of the Workup for Carboxylic Acid (IV)

A. sample was removed from the batch and cooled to 6°C and very thick slurry was formed. Acetonitrile (4 vol) was added, which dissolved the majority of the solid material, and the mixture was again concentrated to four volumes. Upon cooling to 6°C,

and holding for one hour, the sample formed well behaved slurry. The product was collected by filtration, washed with water and dried to give acid 3 as an off—white solid in 95.3% purity (AUC, HPLC).

The remainder of the reaction mixture was worked up as described in the above procedure to give carboxylic acid (IV) in 77% yield containing 7.0 wt % IPAc. This compares with the previous cGMP result for preparation of acetonide (III) of 85% yield containing 7.4 wt % (IPAc).

The oxidation reaction was repeated and carboxylic acid (IV) was isolated by crystallization from water/acetonitrile as described for the sample above. On this occasion, the reaction mixture did not decolorize during the initial acetonitrile/water strip (Step 8 in the above *Outline*) and carboxylic acid (IV) was isolated as a gray solid in 78% yield and 97.9% purity (AUC, HPLC). Such "non-decolorization" behavior, tentatively ascribed to running the oxidation reaction at <25 °C, was observed during preparation of a previous cGMP batch of IB-MECA and did not impact the quality of the API produced. Karl Fischer analysis indicated the batch contained 0.19% water.

2.2 Control of delayed exotherm in the preparation of carboxylic acid (IV)

The oxidation of acetonide (III) was accompanied by a delayed exotherm, following addition of sodium periodate. Interruption of active cooling results in rapid warming of the batch from 5 to 30°C. This presents a significant safety hazard, particularly upon thither scale-up to fixed manufacturing equipment.

In order to better control the exotherm an inverse addition of the substrate (acetonide (III)) to the mixture of ruthenium trichloride and sodium periodate was preformed. Acetonide (III) (5 g) was added as a solution in acetonitrile-water to the oxidant mixture in water at 30—35°C over two hours. The reaction was complete after 16 hours as regularly observed for the usual mode of addition. Using the improved workup conditions but cooling to 20°C instead of 5°C, acid 3 as a white solid in 62% yield and 99.3% purity (AUC, HPLC). A second crop of material was isolated by filtration of the mother liquors, where further crystallization had occurred, washing with water and drying afforded acid 3 as an off-white solid in 19% yield and 98.2% purity (AUC,

HPLC). The combined yield for two crops of acid 3 was 81%. Both crops were suitable for use in the next step (i.e., preparation of IB-MECA acetonide (VI)).

2.3 Optimizing the conditions for carboxylic acid (IV)

Acetonide (III) (25 g) was converted to carboxylic acid (IV) employing the inverse addition of the substrate to the oxidizing mixture. When the oxidation was complete, the batch was filtered to remove inorganic impurities and the filter cake was washed with acetonitrile (6 vol). The filtrate was diluted with additional water (3 vol) to give a solution of carboxylic acid (IV) in acetonitrile (approximately 21 vol) and water (approximately 7 vol) The batch was concentrated by vacuum distillation at 26—36°C to eight volumes. The estimated acetonitrile-water ratio at this point was 40:60 respectively. The batch was cooled to 5—10 °C to induce crystallization and aged for one hour. The product was collected by filtration, washed with water and dried to give acid 3 as a white solid in 75% yield and 99.75% purity (AUC, HPLC).

This optimized process eliminated the need for an extractive workup, use of THF and IPAc, one filtration and four evaporations to dryness. The cycle time for isolation of carboxylic acid (IV) was significantly reduced and the product was isolated in an easily handled form. When corrected for IPAc content, the yields for the existing and newly developed procedures were comparable (77 versus 75% respectively) and carboxylic acid (IV) was isolated in higher purity by crystallization from acetonitrile-water (97.9—99.7%).

3. Process for the preparation of IB-MECA acetonide (VI)

Carboxylic acid (IV) is converted to IB-MECA Acetonide (VI) over three steps as outlined below. Carboxylic acid (IV) was first converted to acid chloride by treatment with thionyl chloride in acetonitrile, then to amide (V) by reaction with methylamine in the presence of diisopropylethylamine (DIPEA). Coupling of amide (V) with 3-iodobenzylamine hydrochloride gives IB-MECA Acetonide (VI). Intermediates acid chloride and amide (V) are not isolated.

3.1 Purification of 3-iodobenzylamine hydrochloride

The quality of 3-iodobenzylamine hydrochloride had significant impact on the outcome of the synthesis. In particular, 3 hydrochloride, an impurity present in 3-iodobenzylamine hydrochloride, and impurities derived thence, were known to persist during downstream processing including the API. An upper limit of ≤0.5% was established for 3 bromobenzylamine hydrochloride in 3-iodobenzylamine hydrochloride for the successful preparation of IB-MECA. Since a suitable commercial supply of 3-iodobenzylamine hydrochloride was not available for the optimization work, methods for purification were investigated.

A solubility study was performed on 3-iodobenzylamine hydrochloride using the solvents employed in the synthesis of IB-MECA the results of which are outlined in Table 1 below. 3-Iodobenzylamine hydrochloride recrystallized from protic solvents but was insoluble in aprotic organic solvents. No purity enhancement was observed during hot (reflux) slurries in aprotic organic solvents.

Table 1 - Solubility Study on 3-iodobeuzylamine hydrochloride

	Solvent	*Solvent Volumes*	*Behavior at 21C*	*Behavior at reflux*	*Comments*
1	MeOH	1	Insoluble	Soluble	Recrystallized, no purity enhancement
2	MeCN	5	Insoluble	Insoluble	Hot slurry did not enhance purity
3	IPAc	10	Insoluble	Insoluble	Hot slurry did not enhance purity
4	IPA	10	Insoluble	Soluble	Recrystallized, no purity enhancement
5	THF	10	Insoluble	Insoluble	Hot slurry did not enhance purity

Recrystallization from water (4 vol) reduce the level of 3- bromobenzylaniine hydrochloride in 3-iodobenzylamine hydrochloride to within acceptable levels. In order to generate a supply for use in the proof-of-concept run 3-iodobenzylamine hydrochloride (150 g, ex. Apin) was recrystallized from water in 78.6% yield. The concentration of 3-bromobenzylamine hydrochloride was reduced from 0.92% to 0.38%.

A batch of carboxylic acid (IV), prepared using the modified conditions, was converted to IB-MECA acetonide (VI) using the procedure *outlined* below. All reagent, weight and volume equivalents are quoted with respect to the input of carboxylic acid (IV).

1. The carboxylic acid derivative of formula IV (1 wt equiv) was mixed with acetonitrile (10 vol) which formed a heavy slurry and the heavy slurry was agitated at 20°C-25°C;

2. To the agitated slurry a halogenating agent, namely, thionyl chloride (1.6 equiv) was added and the mixture was stirred for at least one hour to form a solution;

3. The reaction was monitored for completion by TLC eluting with IPAc-MeOH (10:1).

4. The reaction solution was concentrated to an oil (to remove the thionyl chloride) by rotary evaporation at 20°C (bath temperature).

- Acetonitrile (0.5 vol) was addeded and the mixture was concentrated to oil once more. This oil comprised concentrated acid chloride.

5. The acid chloride was re-dissolved in acetonitrile (10.4 vol) and cooled to <2°C while stirring.

6. Methylamine (2M solution in THF, 1.05 equiv) was added and the mixture temperature was maintained at <5°C. A white precipitate (suspected methylamine hydrochloride) was observed in the reactor.

7. the product was stirred at <5°C for at least 15 minutes.

8. DIPEA (1.5 equiv) was then added and the temperature of the system was maintained at <5°C.

9. Active cooling was discontinued and the reaction mixture was allowed to warm to 20°C over approximately two hours.

10. The reaction was monitored for completion by TLC eluting with IPAc-MeOH (10:1). When complete, a solution of amide (V) in MeCN/THF was obtained.

11. To the solution of amide (V) 3-iodobenzylamine hydrochloride (1.35 equiv) was added followed by DIPEA (5.0 equiv).

12. The mixture was heated to 70°C and monitored for reaction completion by HPLC. The expected reaction time was 14—16 hours and the completion condition was ≤0.7% amide (V) remaining.

13. When completed, the product was cooled to <40°C and concentrated to an oil by rotary evaporation. foaming at this point was especially avoided.

14. The residue was then dissolved in IPAc (8 vol).

15. to the dissolved residue saturated aqueous $NaHCO_3$ (7 vol) was added and the mixture was agitated for at least 30 minutes.

16. Stirring was then stopped to allow settling, and separation of the phases.

17. The organic phase was washed with water (4 vol).

18. The combined aqueous phases were back extracted with IPAc (2 x 3.4 vol).

19. The organic extracts were combined and concentrated to a residue by rotary evaporation.

20. The product was then slurried in MeOH (4 vol) then concentrated to a residue by rotary evaporation.

21. MeOH (4 vol) was then added to the product of step 20 and heated to dissolution (approximately 65°C) with stirring.

22. the product of step 21 was then coolied to <30°C to induce crystallization.

23. The crystallized product was then collected by filtration and the filter cake was washed with chilled (13°C) MeOH (1.8 vol).

24. The cake was dried at 30°C-40°C in vacuo to give IB-MECA acetonide (VI).

25. The recrystallization from MeOH and drying was repeated as necessary to obtain IB-MECA acetonide (VI) within release specifications. Expected yield was 48%.

IB-MECA acetonide (VI) was isolated as a white solid in 80% yield and 99.52% purity (AUC, HPLC) after a single recrystallization from methanol. The impurity derived from 3-bromobenzylaine hydrochloride was observed at a concentration of 0.21% (specification: ≤0.5%) and all other impurities were <0.1%. These results demonstrated that the modifications used to prepare acetonide (III) and carboxylic acid (IV) produced material which was suitable for use in the preparation of IB-MECA acetonide (VI). They also implied that use of higher quality acid 3 (98.2—99.3% purity, previously 92—93%) allowed preparation of IB-MECA acetonide (VI) in very high purity without the need for multiple recrystallizations. HPLC data also indicated that amide (V) can be successfully purged from an IPC concentrationof up to 2.3% during isolation of IB-MECA acetonide (VI).

4. Process for the preparation of IB-MECA (I)

IB-MECA (I) was prepared by deprotection of IB-MECA acetonide (VI) using aqueous hydrochloric acid.

The batch of IB-MECA acetonide (VI) above was deprotected, using the method steps outlined below (Steps 1—10), to give IB-MCA (I) as a white solid in 90% yield and 99.67% purity (AUC, HPLC). The concentration of the impurity derived from 3-bromobenzylamine hydrochloride was 0.18% and no other impurities were >0.1%.

1. IB-MECA acetonide (VI) (1 wt equiv) and THF (5 vol) were added to a reactor.

2. Agitation was initiated followed by the addition of 1N hydrochloric acid (5 vol). The mixture warmed from 16°C to 25°C.

3. Then, the mixture was actively heated to 50°C and reaction completion was monitored by HPLC. Completion condition: ≤1.5% acetonide remaining. The expected reaction time was eight hours. If not complete after eight hours, the batch temperature was lowered to 40°C to avoid formation of impurities.

4. The product was filtrated at 40°C.

5. The filtered product was then cooled to at least 15°C then quenched into saturated $NaHCO_3$ (15 vol) maintaining temperature at 10°C - 25°C. The product precipitated on contact with the base.

6. The mixture was stirred at 10°C - 25°C for at least 12 hours.

7. The solids were collected by filtration and the filtered cake was rinsed with H_2O (5 x 0.95 vol).

8. The washed product was then slurred in methanol-water (9:1, 9.9 vol) at 50°C for at least 30 minutes then cooled to 15°C - 25°C.

9. The product was collected by filtration and the filter cake was washed with methanol-water (9:1, 0.27 vol).

10. The product was dried at 30°C - 40°C *in vacuo* to give IB-MECA (I), expected yield was 81%.

11. The product was re-slurred in water (4.14 vol) at 35°C - 45°C for at least three hours.

12. The re-slurred product was then cooled to 25 °C then collected by filtration.

13. The filtered cake was washed with water (2 x 1 vol).

14. The washed cake was then dried at 55°C - 65°C to give IB-MECA (I). Expected recovery was 78%.

EXAMPLE 2: Proof-of-Concept for large scale synthesis of IB-MECA (I)

In order to demonstrate the optimized conditions developed for the synthesis of IB-MECA (I) from 6-chloropurine-9-riboside (II), the procedures above were preformed

for the preparation of 50 g of IB-MECA (I). Thus, 6-chloropurine-9-riboside (II) was converted to acetonide (III) using the method described below. All reagent, weight and volume equivalents are quoted with respect to the input of riboside

Optimized Method for preparation of acetonide (III)

1. Riboside (II) (1 wt equiv) was added to a reactor followed by the addition of acetone (23 vol) and agitation.
2. To the reactor TsOH (0.05 equiv) was then added followed by 2,2-dimethoxypropane (3.5 equiv).
3. The mixture was stirred at 20°C - 25°C for 48—96 hours and tested for reaction completion by HPLC. Completion condition: riboside NMT 2%.
4. The reaction was quenched by addition of 1 N NaOH (0.052 equiv) and stirring for one hour.
5. The product was concentrated by rotary evaporation (30°C - 40 °C) to nine volumes.
6. Water (9 vol) was then added.
7. The product was then concentrated by rotary evaporation (30°C - 40 °C) to 12.5 volumes.
8. The mixture was cooled to 0°C - 5°C; and maintained at 0°C - 5°C for at least one hour.
9. Collect the product by suction filtration, followed by rinsing with cold (0°C - 5°C) H_2O/acetone (2:1, 1.5 vol).
10. The product was then dried at 40°C to give acetonide (III). Expected yield was 79%.

Acetonide (III) was isolated as a white solid as pale yellow crystals in 82.2% yield (153.1 g) from 6-chloropurine-9-riboside (II)(163.3 g) in 99.58% purity (AUC, HPLC). The reaction was complete after 63 hours (Step 3 in *Outline* above) and was held overnight (14 hours) at the end of Step 7. The temperature of the batch immediately prior to filtration in Step 9 (in *Outline* above) was 2°C and the drying time was 17 hours. No processing issues were encountered in the running of the batch. Acetonide (III) (147.2 g) was carried forward and converted to acid 3 using the method described below. All

reagent, weight and volume equivalents are quoted with respect to the input of acetonide (III).

Optimized method for preparation of carboxylic acid (IV)

1. $NaIO_4$ (2.30 equiv), TBAI (1 mol %) and water (2 vol) was added to a reactor and stirred to form a slurry.
2. $RuCl_3$ (1.6 mol %) was added and the weighing vessel was rinsed with water (1 vol).
3. The reactor mixture was heated to 30 °C with stirring.
4. Acetonide (III), as a solution in acetonitrile (12 vol) and water (1 vol) were charged to the reaction mixture and the temperature was maintained at 30°C-35°C. The addition was expected to take two hours to complete. When the addition is complete, the vessel which contained the acetonide (III) solution with acetonitrile (3 vol) was rinsed and add to the product.
5. The mixture was cooled at 30°C - 35 °C and monitored for reaction completion by TLC. The expected reaction time is 16 hours.
6. the product was cooled at 20°C - 25 °C and filtered to remove inorganic impurities.
7. The reactor and filter cake were rinsed with acetonitrile (6 vol) and the filtrates were diluted with water (3 vol).
8. The filtrates were concentrated to eight volumes by rotary evaporation at 25°C-35 °C. At this stage the produce decolorized by evaporation of volatile RuO_4.
9. The product was cooled to 5°C - 10 °C to induce crystallization and aged for at least one hour.
10. The product was then collected by filtration and the filter cake was washed with water (3x3vol).
11. The product was dried at 35°C - 45 °C in vacuo to give acid (IV). Expected yield is 75%.

Acetonide (III) was charged to the reaction mixture over three hours and reached a maximum batch temperature of 36°C. The oxidation was complete after 14 hours (TLC analysis). Upon cooling to 20°C - 25 °C (Step 6 in *Outline* above) the batch unexpected

darkened, changing from orange to green, indicating a change in the oxidation state of the ruthenium species from Ru^{VI} to Ru^{III}. Also, the batch did not decolorize during the concentration to reduce the concentration of acetonitrile. Acid (IV) was ultimately isolated as a dark green solid in 63% yield (96.2 g) and 98.9% purity (AUC, HPLC). Since previous studies had shown that the color causing impurities were purged during downstream processing the product was carried forward without further purification. Carboxylic acid (IV) (75 g) was converted to IB-MECA acetonide (VI) using the method described in Example 1.

The chlorination reaction, to prepare acid chloride, was complete after 70 minutes (Step 3 in *Outline* in Example 1) and the batch foamed considerably during concentration (Steps 4 and 5 in Example 1). Methylamine (2M solution in THF) was added to the acid chloride solution over 16 minutes and the maximum batch temperature was 5°C. Conversion of acid chloride to amide (V) was complete after two hours during which time the batch warmed from 5°C to 17°C (Steps 10 and 11 in Example 1). Coupling of 3-iodobenzylamine hydrochloride with amide (V) required 16 hours to reach completion (Step 13 in Example 1). During the extractive workup, a significant quantity of solid material was observed. At Step 17 (in Example 1) excess $NaHCO_4$ precipitated from the mixture and can be overcome by the addition of more water During Step 18 (in Example 1) the product precipitated and required the addition of water (5 vol) and IPAc (5 vol) to redissolve IB-MECA acetonide (VI). HPLC analysis of the aqueous layer at the end of Step 18 (in Example 1) indicated that IB-MECA acetonide (VI) was not present in a significant concentration. As such, the back-extractions of the aqueous phase with IPAc (Step 19 in Example 1) were omitted. IB-MECA acetonide (VI) was ultimately isolated as a pale green solid in 75.2% yield (91.6 g) and 99.79% purity. The "bromo-impurity", present in 3-iodobenzylamine hydrochloride at 0.38%, was observed at a relative concentration of 0.21%. The batch was significantly but not completely decolorized (input carboxylic acid (IV) was dark green) at the end of the isolation procedure.

IB-MECA acetonide (VI) (85 g) was deprotected, using the method outlined in Example 1, to give IB-MECA (I) as a white solid in 84.5% yield (67 g) and 99.83% purity. The acetonide cleavage was complete after 9.5 hours (Step 3 in Example 1) and the product decolorized during collection after the methanol-water slurry (Step 9 in

Example 1). After the slurry in water to remove residual methanol, the product filtered very slowly and was transferred to the dryer with great difficulty. The purity of IB-MECA was unchanged between its initial isolation from methanol-water and after re-slurry from water.

EXAMPLE 3: cGMP production of IB-MECA (I)

cGMP Manufacture of 6-Chloropurine-9-riboside Acetonide

To a 200-L reactor with moderate stirring were charged acetone (115 L, 23 vol) and 6-chloropurine-9-riboside (5.0 kg, 17.4 mol, 1.0 wt/1.0 vol). Subsequently, *p*-TsOH•H_2O (166 g, 0.88 mol, 0.05 equiv, 0.033 wt) and 2,2-dimethoxypropane (7.6 L, 62 mol, 3.54 equiv, 1.52 vol) were added and the resulting yellow suspension stirred at ambient temperature. After 45 h, a sample of the resulting yellow-green solution was taken and analysis by HPLC revealed the starting material to be present at 0.42% by conversion (overall purity 96.9 area %). The batch was neutralized by the addition of 1N NaOH (900 mL, 0.90 mol, 0.05 equiv, 0.18 vol). This addition took approximately 2 min; the final pH was pH 7. The batch was allowed to stir for 1 h. The resulting cloudy yellow mixture was concentrated under reduced pressure at 35 ± 5 °C on the rotary evaporator over a period of 8 h, until a volume of 45 L (9.0 vol) was achieved. The concentrate was stored under N_2 at 2–8 °C.

The concentrate was transferred to a 200-L reactor and stirring commenced. Water (45 L, 9.0 vol) was added and the resulting dilute suspension was stirred for 55 min. The batch was transferred portionwise to a 72-L reactor assembled in a heating mantle equipped for vacuum distillation. Distillation at 35 ± 5 °C commenced and proceeded until a batch volume of 62 L (12.4 vol) was achieved (The distillation was conducted over a period of two days, and included 15 hours of aging at ≤30 °C once complete). The batch was transferred to a 72-L reactor assembled in a cooling bath. The batch was chilled over a period of 4½ h until the temperature reached ≤5 °C and was stirred for an additional 1 h. The solids were filtered employing Sharkskin filter paper and the cake was rinsed with chilled 2:1 water/acetone (7.5 L, 1.5 vol) (The total filtration time was approximately 1 hour 40 minutes and included pulling N_2 through the cake in order to help it dry). The damp solids (5.99 kg) were transferred into six glass

drying trays and dried under vacuum in an oven at 40 ± 5 °C. After drying for 47 h, the batch was packaged in 4-mil LDPE (double bags) under N_2 and stored in a fiber drum. This afforded 6-chloropurine-9-riboside acetonide (4505 g, 79%).

cGMP Manufacture of IB-MECA Acetonide

To a 72-L reactor supported in a cooling bath, was charged CH_3CN (37 L, 14.8 vol). Stirring commenced at ambient temperature. To this was added 6-chloropurine acetonide (2234 g and 266 g, total = 2500 g = 1.0 wt = 1.0 vol, 7.65 mol), ruthenium(III) chloride hydrate (25 g, 0.121 mol, 0.016 equiv, 0.010 wt), water (10 L, 4.0 vol), and TBAI (25 g, 0.068 mol, 0.009 equiv, 0.010 wt). The resulting mixture was cooled to 5°C over 1 h employing an ice-water cooling bath, and $NaIO_4$ (3750 g, 17.5 mol, 2.3 equiv, 1.5 wt) was added over 2 min while maintaining the internal batch temperature <10 °C. The ice/solvent bath was emptied after 50 min and the batch was allowed to warm to ambient temperature (The batch temperature reached a maximum of 33 °C over a period of two hours. A cold-water bath was applied to prevent the batch temperature from exceeding this temperature). The resulting thick brown-orange suspension was stirred at 15–30 °C for 21 h. Analysis by TLC (IPAc, UV detection) showed the disappearance of the 6-chloropurine-9-riboside acetonide. The yellow suspension (21°C) was filtered over a period of 30 min until dripping ceased; CH_3CN (15 L, 6.0 vol) was employed as a rinse of the reactor and cake. The filtrate was concentrated in three portions on the rotary evaporator with the water bath set at 40±5°C over a period of 11 h.

To a 72-L reactor were charged the resultant residue (7.7 kg) and purified water (22.5 L, 9 vol). Stirring at ambient temperature was commenced. After 1 h, the batch (23 °C) was filtered, and the reactor and the cake were rinsed with purified water (7.5 L, 3 vol). The damp cake (4.7 kg) was transferred to six drying trays and dried in the vacuum oven set at 40 °C for six days. The IPC KF (specification set at <0.6%) and ^1H NMR (DMSO-d_6) showed acceptable material. This afforded 6-chloropurine acid (2145 g, 82%) which was stored under N_2 in amber glass jars with Teflon lined lids.

Typical Procedure for the Manufacture of Crude IB-MECA Acetonide

To a 72-L reactor, was charged 6-chloropurine acid [2600 g, 7.63 mol, 1.0 wt=1.0 vol] using CH_3CN (31.7 L, 12.2 vol) to effect the transfer, and stirring commenced.

Thionyl chloride (889 mL, 12.2 mol, 1.60 equiv, 0.342 vol) was added to the thick gray slurry and the mixture stirred at <30°C for 4h. Approximately 0.5 mL of the resultant dark solution was added to MeOH (2 mL, HPLC grade, Fisher), and analysis by TLC (UV detection, IPAc/MeOH, 10:1) showed the disappearance of the starting material. Over a period of 6.5 h, the batch solution was concentrated under vacuum on the rotary evaporator until distillation ceased (the water bath was initially set at 25 ± 5 °C and gradually increased to 35 ± 5 °C for this); CH_3CN (825 mL, 0.32 vol) was used to rinse the reactor. The water-bath heat source was switched off and CH_3CN (7.6 L, 2.9 vol) added to the residue in the bulb. Without vacuum, the bulb was rotated until the batch became fully mobile and then it was transferred to a 72-L reactor positioned in a steel tub. Stirring was commenced and additional CH_3CN (25.5 L, 9.8 vol) was added. The batch was cooled using an ice-water/solvent bath until the internal batch temperature was <2 °C (this took 1 h); then 2 M methylamine in THF (4004 mL, 8.01 mol, 1.05 equiv, 1.54 vol) was added via a 5-L addition funnel over a period of 52 min while maintaining the internal batch temperature <7 °C. Subsequently, DIPEA (1976 mL, 11.3 mol, 1.5 equiv, 0.76 vol) was added via a 5-L addition funnel over 1 h; stirring was continued at <7 °C for a minimum of 1 h, the cooling bath was drained, and stirring continued for 11 h while the batch was allowed to warm to ambient temperature (the pH of the batch was 9). Typically the minimum temperature of the batch for these operations was 0 °C. Analysis by TLC (UV detection, IPAc/MeOH, 10:1) showed the disappearance of the 6-chloropurine acid/acyl chloride and the formation of one higher-running major product. The batch was transferred to another 72-L reactor setup in a heating mantle, equipped with a water-cooled condenser; CH_3CN (1.3 L, 0.5 vol) was used to aid with the transfer. Stirring was commenced and 3-iodobenzylamine•HCl (2777 g, 10.30 mol, 1.35 equiv, 1.068 wt) was added. Subsequently, DIPEA (6656 mL, 38 mol, 5.0 equiv, 2.56 vol) was added and the mixture heated at 70 ± 5 °C for 25 h. Analysis by HPLC showed 0.70% of the 6-chloropurine amide remaining by conversion, thus just meeting the ≤0.70% specification. The heat source was switched off and the batch allowed to cool overnight. Over a period of 8 h, the batch was concentrated under vacuum on the rotary evaporator at 40 ± 5 °C until distillation ceased; CH_3CN (1650 mL, 0.63 vol) was used to rinse the reactor. With the aid of IPAc (5.36 L, 2.1 vol), the residue was transferred to a 72-L

reactor. Additional IPAc (20.4 L, 7.85 vol) was added to the reactor and stirring initiated. To this was added saturated aqueous sodium bicarbonate (22.2 L, 8.5 vol). After 30 min of stirring, the biphasic system was allowed to settle for 10 min and the lower aqueous phase collected (additional water (5 L) was added to dissolve the minor amount of remaining solids in the biphasic mixture). The remaining organic phase was washed with water (12.7 L, 4.9 vol) with 25-min stirring time and 38-min settling time. The combined organic phase was concentrated under vacuum on the rotary evaporator at 40 ± 5 °C until distillation ceased (over a period of 6 h). The carboy was rinsed with IPAc (825 mL, 0.32 vol). In stages the resulting residue was slurried in the rotary evaporator bulb with MeOH (12.7 L, 4.9 vol) and concentrated until distillation ceased (4.5 h). This afforded crude IB-MECA acetonide (7.2 kg) as a damp beige solid which was stored for further processing and batch combination. Analysis by HPLC showed IB-MECA acetonide at 91.3 area % purity.

Purification of Crude IB-MECA Acetonide

The crude MeOH damp IB-MECA acetonide (15 kg, 91 area %) was recrystallized from MeOH (34 L) at 60–65 °C. The resulting filter cake was rinsed with chilled MeOH (15.3 L) and transferred to eight drying trays (batch weight 10 kg) Analysis by HPLC showed IB-MECA acetonide at 65 area % purity present in the filtrate. It was estimated from the peak height that 1 kg of this material was sacrificed to this operation. The batch was dried in the vacuum oven set at 40 °C for approximately 22 h (7945 g). Analysis by HPLC showed the desired product at 99.0 area % purity contaminated with two significant impurities at RRT 0.64 (0.32 area %) and RRT 1.30 (0.58 area %). The mass spectra of these peaks are:

RRT= 0.64

MW = 424.19

m/e: 424.19 (100%), 425.19 (23.9%), 426.19 (4.0%), 425.18 (2.2%)

C, 59.42; H, 5.70; N, 19.80; O, 15.08.

RRT 1.30

MW=752.34 gr/mol

m/e: 752.01 (100.0%), 753.01 (32.4%), 754.02 (4.5%), 754.01 (1.5%)

C, 43.10; H, 3.48; I, 33.74; N 11.17; O 8.51

This material was recrystallized again from MeOH (23.8 L) at 60–65 °C. The resulting filter cake was rinsed with chilled MeOH (2 × 8 L). The total filtration time was 85 minutes. The cake was stored under a flow of N_2. Analysis of the cake by HPLC showed the desired product at 99.77 area % purity contaminated with two significant minor impurities at RRT 0.64 (0.07 area %) and RRT 1.30 (0.16 area %). The batch was transferred to six drying trays (batch weight 7.4 kg) rather than perform the third optional recrystallization. The batch was dried in the vacuum oven set at 40 °C for approximately 60h. This afforded IB-MECA acetonide (7097 g) as a white solid after packaging into four amber glass jars; storage was at ambient temperature.

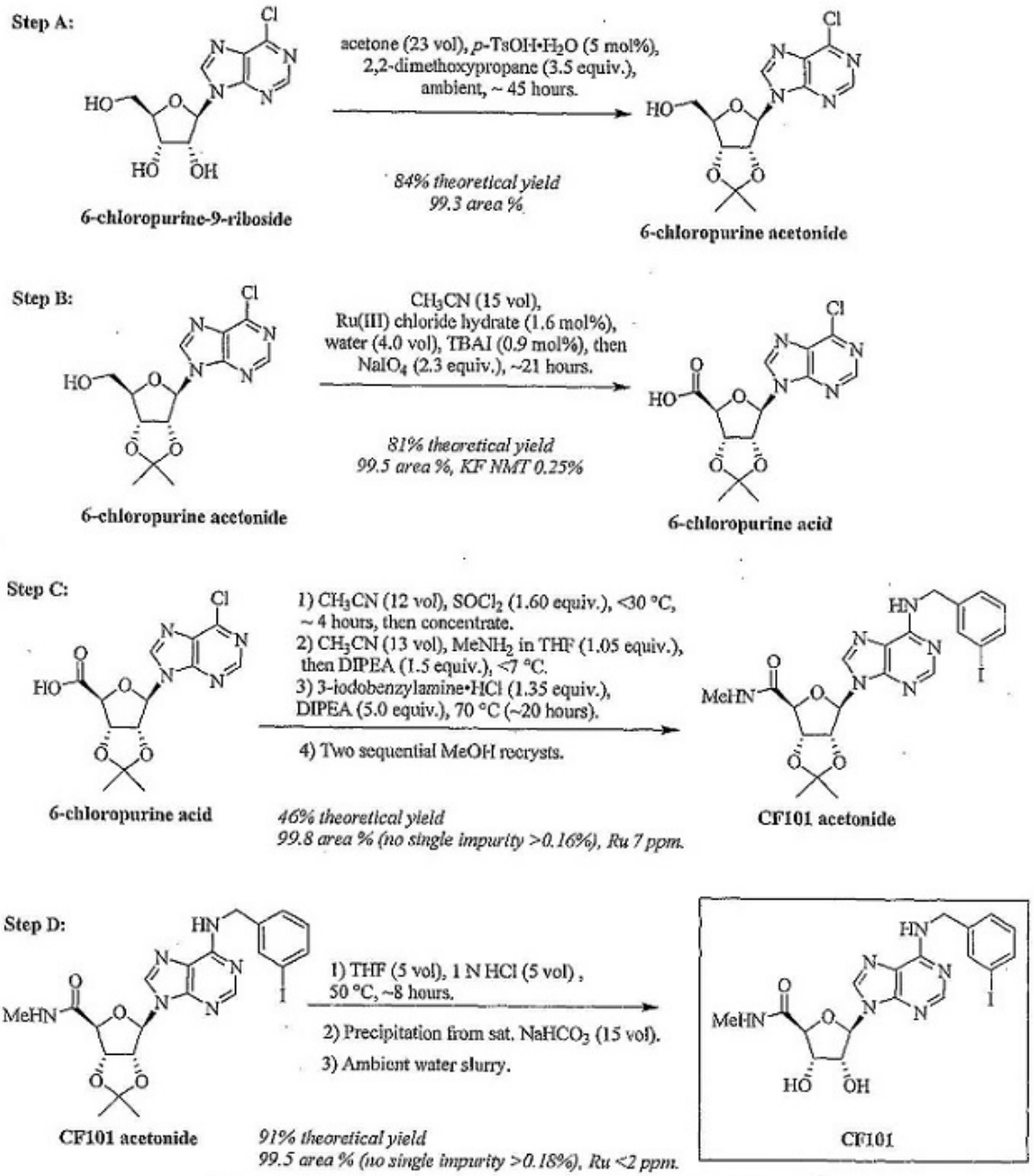
cGMP Manufacture of IB-MECA

To a 72-L reactor were charged THF (18.1 L, 5.1 vol), IB-MECA acetonide (3.55 kg, 6.45 mol, 1.0 wt/1.0 vol), and 1N aqueous HCl (17.8 L, 17.8 mol, 2.76 equiv, 5.0 vol). The resulting pale green stirring slurry was heated at 50 ± 5 °C for approximately 8 h at which point HPLC analysis showed 1.16% of IB-MECA acetonide remaining wrt IB-MECA (thus meeting the specification ≤1.5%). The batch was allowed to cool to approximately 40 °C and then filtered through an in-line filter via a transfer pump. The emptied reactor and the transfer line were rinsed with THF (600 mL, 0.17 vol). The resulting filtrate was stored in the cold room (2–8 °C) overnight. To a 200-L reactor was added chilled saturated aqueous $NaHCO_3$ (53.6 L, 15 vol, 16 °C) through an in-line filter and stirring commenced. The IB-MECA rich filtrate (15 °C) was added over 30 min to the 200-L reactor via a transfer pump equipped with an in-line filter. The resulting white precipitate was stirred overnight to age (there was little temperature fluctuation during the precipitation which occurred at 20 ± 2 °C, no cooling was applied, and there was a minor amount of foaming. The pH of the slurry was pH 7.5). The batch was filtered using a nylon filter cloth; the emptied reactor and the cake were rinsed with water (5 × 3.4 L, 4.8 vol). The cake was pulled under a flow of N_2 (total filtration time was 5.5 h), packaged for further processing, and stored in the cold room. This batch (9.2 kg wet weight) was shown to be 99.5 area % pure with no single impurity >0.20 area % by HPLC.

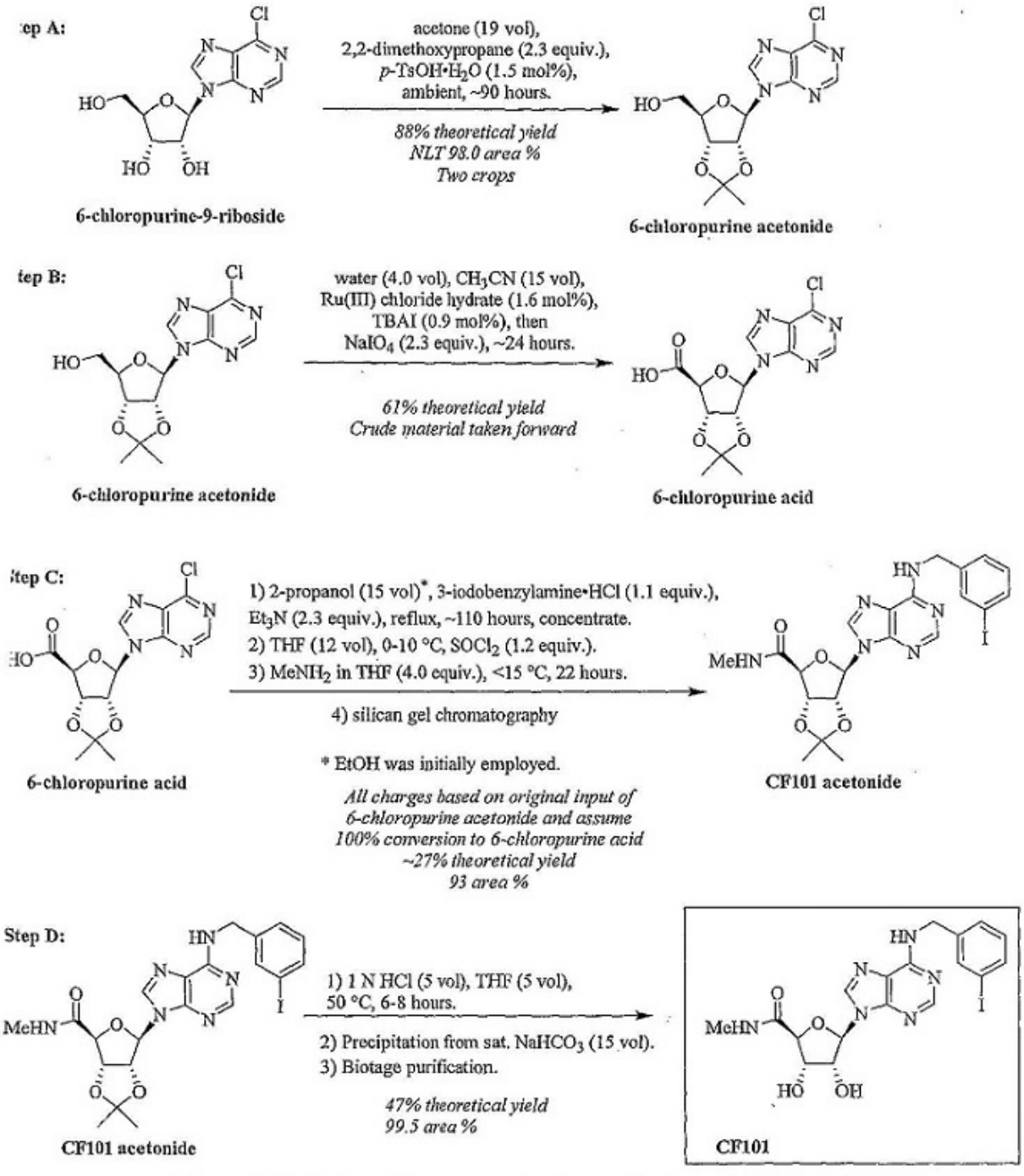
EXAMPLE 4: Comparative Kilo-Scale cGMP Production Processes of IB-MECA

Scheme 1 represents the procedures employed for a kilo-scale preparation of IB-MECA in accordance with the present disclosure and as defined in the appended claims (typical yields and HPLC purities are shown). The production steps represented in Scheme 1 are similar to the production processes for the preparation of IB-MECA detailed in Example 1 above. A single batch production of IB-MECA using this process was as much as 6 kg (99.5 area % pure by HPLC, with no single impurity >0.18%). The cGMP production started with the commercially available 6-chloropurine-9-ribososide (10 kg) and afforded IB-MECA (6 kg, 34% overall theoretical yield (60 wt %)).

Scheme 2 represents a variation in the production process of IB-MECA (typical yields and HPLC purities are also shown). The difference resides in the work-ups, order of reactions, equivalents of reagents charged, solvents employed, and subsequent yields. The procedures in Scheme 2 employed both silica gel column chromatograph and reverse phase Biotage purification. The process of Scheme 2 was performed on 350-g and 2-kg scales and afforded IB-MECA (32 g, 9 wt %) and (414g, 21 wt %), respectively.



Scheme 1. Process for the production of IB-MECA (CF101)



Scheme 2. Variation of the process for the production of IB-MECA (CF101)

A number of key differences are noted between the processes steps of Scheme 1 and the processes steps on Scheme 2 employed for the cGMP production of IB-MECA, as follows:

Step A Preparation of 6-chloropurine acetonide:

In the process according to Scheme 2, the amounts added of *p*-TsOH•H_2O and 2,2-dimethoxypropane were increased in order to enhance the reaction rate without adversely impacting yield and quality. This cut the costly reaction-vessel residency time in half. On scale, the initial procedure was inconsistent and led to incomplete reaction. To drive the reaction to completion additional reagents had to be added in portions over a period of up three weeks, and resulted in significant increase in overall reaction volume. These charges were also optimized such that possible side-products were kept to a minimum.

The process according to Scheme 1, which is also subject of the appended claims, afforded high-quality material as a *single crop* in similar yield as achieved for the process of Scheme 2.

Step B Preparation of 6-chloropurine acid:

According to the process detailed in Scheme 1, subsequent reagent and solvent additions in order to afford IB-MECA Acetonide were based upon the isolated weight of the acid. Whereas according to the process of Scheme 2, the addition of reagents and solvents were with respect to the weight of the isolated precursor intermediate (6-chloropurine acetonide). Thus, a slurry, an extractive IPAc/H_2O work-up, and a Na_2SO_4 drying operation were each eliminated in process of Scheme 1.

The acid in Scheme 1 was isolated from water in an easy to handle form, that can be oven dried to meet a residual water content specification (subsequent acyl chloride formation is water sensitive). A tolerable upper limit for residual water in the acid was determined to be <0.6 wt %. This was consistently met by simple vacuum oven drying, without sacrificing quality. The recovery was enhanced by increasing the washing volumes of the filter-cake, and by eliminating the aforementioned redundant processing.

Step C Preparation of IB-MECA Acetonide:

There is a significant difference in the order of the three synthetic transformations (reaction with 3-iodobenzylamine, then acyl chloride formation, and finally amide formation with $MeNH_2$) between the two Schemes. The additions of

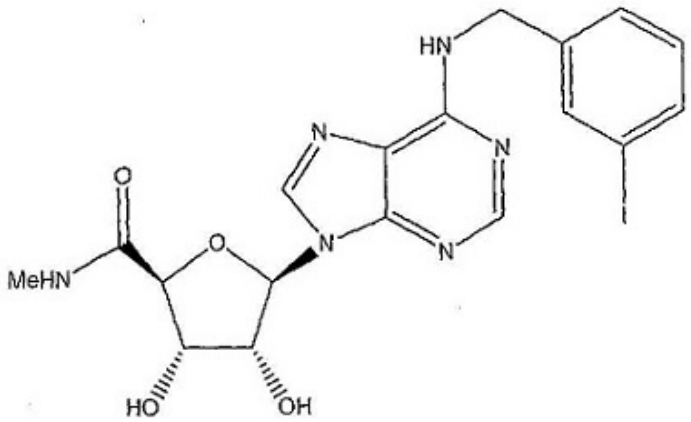
reagents were optimized with respect to the input of 6-chloropurine acid (see step B above). A single reaction solvent (CH_3CN) was used in Scheme 1, for these reactions. This eliminated ester-impurity formation encountered when employing the processes of Scheme 2 (not shown). Additionally, according to the sequence of processes of this step in Scheme 1, the most costly material (3-iodobenzylamine) was employed in the last stage of the synthesis. The silica gel column chromatography purification requirement in the process of Scheme 2, has been replaced with MeOH recrystallizations (scheme 1). There were several other potential process impurities identified at this juncture (not shown).

Step D Preparation of IB-MECA:

Biotage purification employed in the process of Scheme 2 was no longer required, since the purity of the precursor IB-MECA acetonide was improved in Scheme 1, through MeOH recrystallizations. Thermal decomposition was determined to occur during the acetonide deprotection (acidic conditions) in both Schemes, as such the reaction time is limited to 8 hours (without adversely affecting yield).

CLAIMS:

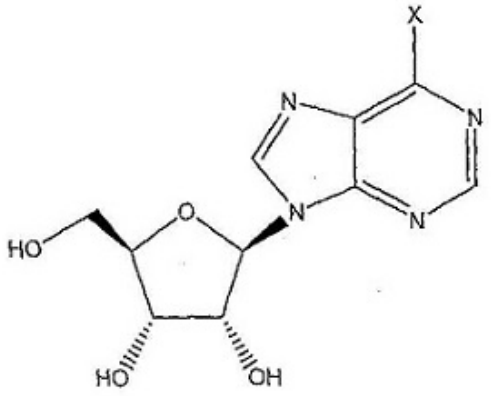
1. A method for the chemical synthesis of IB-MECA, having the following formula (I):



(I)

the method comprising :

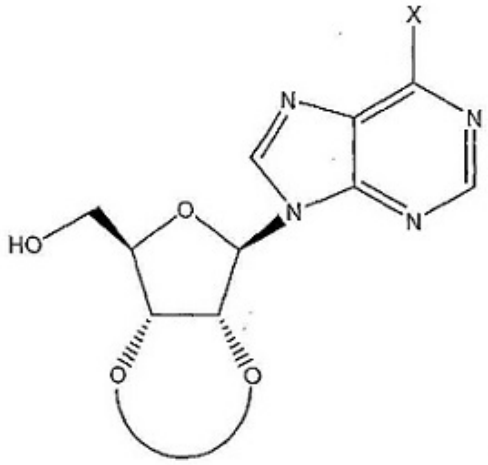
(i) reacting 6-halopurine-9-riboside of the following formula (II):



(II)

wherein X is a halogen selected from Cl, I or Br;

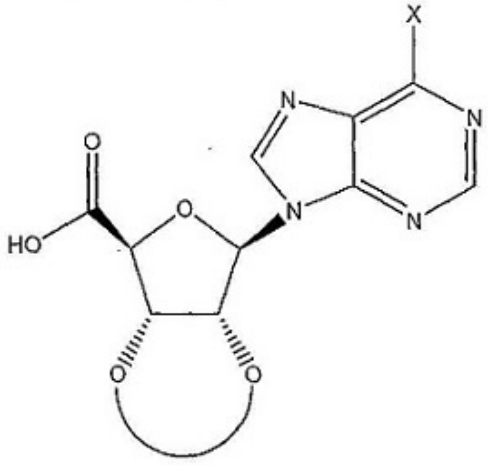
with a diol protecting reagent to obtain a diol protected 6-halopurine of the following formula (III):



(III)

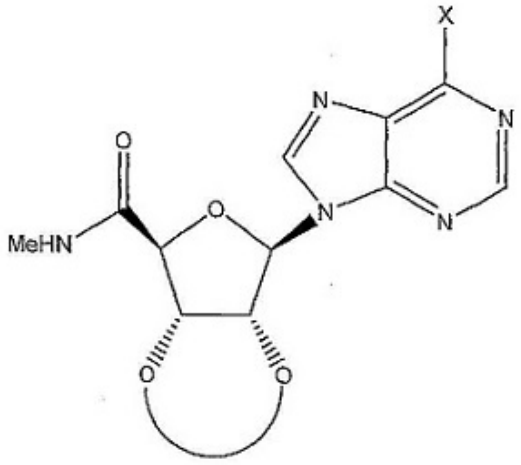
wherein said diol protecting reagent comprises a straight or branched C_1-C_6 alkyl group;

(ii) oxidizing the primary alcohol in said diol protected 6-halopurine of formula (III) to a respective carboxylic acid derivative of formula (IV):



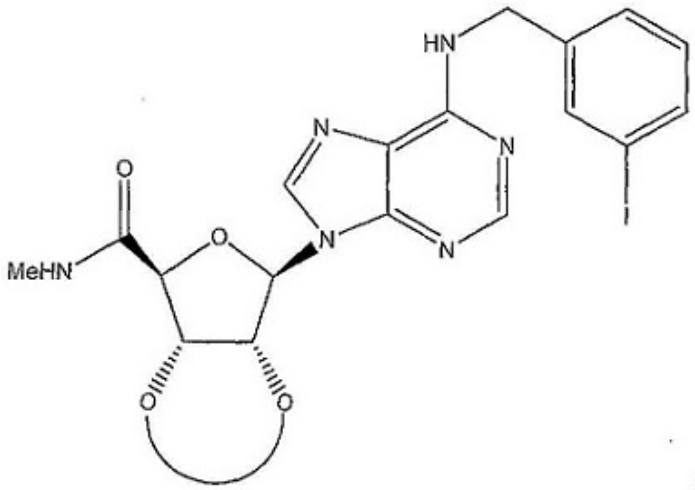
(IV)

(iii) reacting the carboxylic acid group of the derivative of formula (IV) with a methylamine to obtain the respective methylamide derivative of the diol protected 6-halopurine (III), the methylamide derivative having the formula (V):



(V)

(iv) substituting the halogen group of methylamide derivative (V) with 3-iodobenzylamine to form a diol protected IB-MECA having the formula (VI);



(VI)

(v) removing diol protection to obtain said IB-MECA of formula (I).

2. The method of Claim 1, wherein said halogen is chloride.

3. The method of Claim 1 or 2, wherein said protecting group is C_3-C_6 dialkyloxyalkane.

4. The method of Claim 3, wherein said dialkyloxyalkane is 2,2-dimethoxypropane.

5. The method of any one of Claims 1 to 4, wherein said diol protection is achieved in the presence of a strong acid and a polar organic solvent.

6. The method of Claim 5, wherein said strong acid is selected from p-TsOH, methane sulfonic acid, benzene sulfonic acid, formic acid, hydrochloric acid, sulfuric acid.

7. The method of Claim 5, wherein said polar organic solvent is a water-miscible solvent.

8. The method of Claim 7, wherein said polar organic solvent is acetone.

9. The method of any one of Claims 1 to 8, wherein said oxidation of the primary alcohol in said diol protected 6-halopurine of formula (III) to the corresponding carboxylic acid derivative is executed in the presence of a catalytic amount of an oxidizing agent selected from ruthenium metal, ruthenium chloride, chromium trioxide, sodium periodate, potassium dichromate, potassium permanganate, silver oxide, nitric acid, platinum oxide/oxygen, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), sodium chlorite and any combination thereof.

10. The method of Claim 9, wherein said oxidation is executed in the presence of a catalytic amount of $RuCl_3$ and sodium periodate.

11. The method of any one of Claims 1 to 10, wherein conversion of the carboxylic acid derivative of formula (IV) to said respective methylamide derivative of formula (V) is executed by nucleophilic substitution in the presence of an halogenating agent and thereafter introducing said methylamine.

12. The method of Claim 11, wherein said halogenating agent is selected from $SOCl_2$ and PCl_5.

13. The method of any one of Claims 1 to 12, wherein the removal of the diol protecting group is performed in the presence of a strong acid and a polar non-protic solvent.

14. The method of Claim 13, wherein said strong acid is HCl and said solvent is Tetrahydrofurane (THF).

15. The method of any one of Claims 1 to 14, permitting large scale synthesis of IB-MECA.

16. The method of any one of Claims 1 to 15 for Good Manufacturing Production (GMP) of IB-MECA.

17. A chemically synthesized IB-MECA, whenever obtained by the method of any one of Claims 1 to 16.

18. A pharmaceutical composition comprising IB-MECA of Claim 17.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/000360

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07H19/16 A61K31/7076 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07H A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FISHMAN P ET AL: "TARGETING THE A3 ADENOSINE RECEPTOR FOR CANCER THERAPY: INHIBITION OF PROSTATE CARCINOMA CELL GROWTH BY A3AR AGONIST" ANTICANCER RESEARCH, HELENIC ANTICANCER INSTITUTE, ATHENS, vol. 23, no. 3A, 1 May 2003 (2003-05-01), pages 2077-2084, XP008048649 ISSN: 0250-7005 cited in the application abstract page 2078, left-hand column, lines 9,10 -/--	17,18

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 June 2008	03/07/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gohlke, Pascale

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/000360

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	RODENKO ET AL: "Solid phase synthesis and antiprotozoal evaluation of di- and trisubstituted 5'-carboxamidoadenosine analogues" BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 14, no. 5, 1 March 2006 (2006-03-01), pages 1618-1629, XP005257043 ISSN: 0968-0896 Scheme 2 page 1619, left-hand column, last paragraph	1-16
X	page 1621; compound 12I	17,18
Y	GALLO-RODRIGUEZ C ET AL: "Structure Activity Relationships of N6-Benzyladenosine-5'-uronamides as A3 Selective Adenosine Agonists" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 37, no. 5, 4 March 1994 (1994-03-04), pages 636-646, XP002136400 ISSN: 0022-2623 page 637; figure 2 page 642, left-hand column, lines 19-35	1-16
X	page 639, right-hand column; table 3; compound 16	17,18
A	AFIFY H M N M ET AL: "A NOVEL AND FACILE REACTION TO N6-ALKYLATED ADENOSINE VIA BENZOTRIAZOLE AS A SYNTHETIC AUXILIARY" JOURNAL OF HETEROCYCLIC CHEMISTRY, HETEROCORPORATION. PROVO, vol. 37, no. 2, 1 March 2000 (2000-03-01), pages 339-341, XP001147847 ISSN: 0022-152X Page 340 - Scheme 1	1-16
X	page 340; compound 8	17,18
P,A	DEVINE ET AL: "An efficient convergent synthesis of adenosine-5'-N-alkyluronamides" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 64, no. 8, 3 December 2007 (2007-12-03), pages 1772-1777, XP022424511 ISSN: 0040-4020 Page 1773 - Scheme 1	1-16
X	page 1774; table 1; compound 9B	17,18

2

SCHEDULE B
SPECIFICATIONS

The current Specifications of the Supplied Product includes the Active Product Ingredient as detailed in the patent "process for synthesis of IB-MECA", International Publication Number: WO 2008/111082.

The final Specifications of the Supplied Product will be detailed and set out in the documents comprising the NDS filing.

SCHEDULE C
PAYMENTS TO CAN-FITE

Part A

Milestone Payments

In consideration of the rights granted to Distributor herein, Distributor will pay to Can-Fite the following non-refundable payments within ten (10) Business Days upon completion of and subject to the following milestones (the "**Milestone Payments**"):

$1,650,000 upon the execution of this Agreement ("**Initial Milestone Payment**");

Receipt of regulatory approval by Health Canada for the Product and first delivery of commercial launch quantities of Product according to a Firm Order as follows:

(i) $1,000,000 upon the first approved indication for either (i) the treatment of Psoriasis or (ii) the treatment of Rheumatoid Arthritis.

(ii) $1,000,000 upon the second approved indication for either (i) the treatment of Psoriasis or (ii) the treatment of Rheumatoid Arthritis.

Part B

Transfer Price

The Transfer Price for Product shall be payable within thirty (30) days of the date of Distributor's receipt of such Product shipment.

Part C

Royalty Payments to Can-Fite

Within 30 days after the end of each quarter (post First Commercial Sale), the Distributor shall (A) deliver to Can-Fite a Certificate of Distributor's Chief Financial Officer as to the Net Sales of the Distributor recorded during such fiscal quarter and (B) remit to Can-Fite an amount representing Royalty Percentage of Net Sales during such fiscal quarter.

SCHEDULE D
MINIMUM SALES REQUIREMENTS
[...]

Exhibit 8.1

Subsidiaries of Can-FiteBioPharma Ltd.

The following table sets forth the name and jurisdiction of incorporation of our subsidiaries as of March 27, 2015.

Name of Subsidiary	Jurisdiction of Incorporation
OphthaliX Inc.	Delaware
Eye-Fite Limited (wholly owned subsidiary of OphthaliX Inc.)	Israel
Ultratrend Limited	England and Wales

Exhibit 12.1

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER UNDER SECTION 302 OF THE SARBANES-OXLEY ACT

I, Pnina Fishman, certify that:

1. I have reviewed this annual report on Form 20-F of Can-fiteBioPharma Ltd;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: March 27, 2015

/s/ Pnina Fishman

Pnina Fishman, Ph.D.
Chief Executive Officer

Exhibit 12.2

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER UNDER SECTION 302 OF THE SARBANES-OXLEY ACT

I, Motti Farbstein, certify that:

1. I have reviewed this annual report on Form 20-F of Can-fiteBioPharma Ltd;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Dated: March 27, 2015

/s/ Motti Farbstein

Motti Farbstein
Chief Operating and Financial Officer

Exhibit 13.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER UNDER SECTION 906 OF THE SARBANES-OXLEY ACT

Pursuant to 18 U.S.C. Section 1350, as created by Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of CanfiteBioPharma Ltd. (the "Company") hereby certifies to such officer's knowledge that:

(i) the accompanying Annual Report on Form 20-F of the Company for the year ended December 31, 2014 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 27, 2015

/s/ Pnina Fishman

Pnina Fishman, Ph.D.
Chief Executive Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. Section 1350, and is not being filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference to any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Exhibit 13.2

CERTIFICATION OF CHIEF EXECUTIVE OFFICER UNDER SECTION 906 OF THE SARBANES-OXLEY ACT

Pursuant to 18 U.S.C. Section 1350, as created by Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of CanfiteBioPharma Ltd. (the "Company") hereby certifies to such officer's knowledge that:

(i) the accompanying Annual Report on Form 20-F of the Company for the year ended December 31, 2014 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 27, 2015

/s/ Motti Farbstein

Motti Farbstein
Chief Operating and Financial Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. Section 1350, and is not being filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference to any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement on Form F-3 (No. 333 - 199033 and No. 333 - 195124), pertaining to Can-Fite Biopharma Ltd. of our report dated March 27, 2015 with respect to the consolidated financial statements of Can-Fite Biopharma Ltd. and its subsidiary, included in this Annual Report on Form 20-F for the year ended December 31, 2014.

/s/ Kost Forer Gabbay & Kasierer

Tel-Aviv, Israel
March 27, 2015

KOST FORER GABBAY & KASIERER
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