UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 6-K

Report of Foreign Private Issuer Pursuant to Rule 13a-16 or 15d-16
Under the Securities Exchange Act of 1934

For the Month of January 2022

001-36203
(Commission File Number)

CAN-FITE BIOPHARMA LTD.

(Exact name of Registrant as specified in its charter)

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

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F.

Form 20-F ☑ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ____

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ____

On January 5, 2022, Can-Fite BioPharma Ltd. issued a press release entitled "Can-Fite Issues Letter to Shareholders". A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Exhibit Index

Exhibit No.	Description
99.1	Press Release dated January 5, 2022

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: January 5, 2022

By: /s/ Pnina Fishman
Pnina Fishman
Chief Executive Officer

Exhibit 99.1

Can-Fite Issues Letter to Shareholders

- ***Q1 2022: Psoriasis Phase III Data & Commencement of Enrollment in Phase IIb NASH***
- ***H1 2022: Commencement of Enrollment in Phase III Liver Cancer***

PETACH TIKVA, Israel, January 5, 2022 -- Can-Fite BioPharma Ltd. (NYSE American: CANF) (TASE: CFBI), a biotechnology company advancing a pipeline of proprietary small molecule drugs that address inflammatory, cancer and liver diseases, today issued a Letter to Shareholders from its Chief Executive Officer, Dr. Pnina Fishman.

Dear Can-Fite Shareholders,

Beginning in the first quarter of 2022, we expect several significant and value-driving events during the calendar year. We are building upon the solid progress achieved in 2021 which included the completion of a 400-patient Phase III psoriasis study, the design, preparation, and clearance to commence our Phase III liver cancer and Phase II NASH studies, as well as several inventions and patents.

Topline Phase III Psoriasis Data Expected Q1 2022 – Our Comfort™ Phase III study of Piclidenoson enrolled and treated approximately 400 patients with moderate to severe plaque psoriasis. In the first quarter, we expect to announce results from the first 16 weeks of treatment, with the primary endpoint of the study being a statistically significant improvement in achieving a PASI score of 75 in Piclidenoson treated patients vs. placebo. Later in 2022, we expect to announce the study's secondary endpoint at 32 weeks of treatment which is non-inferiority of Piclidenoson vs. Otezla. The study has four treatment arms: Piclidenoson 2 mg, Piclidenoson 3 mg, Otezla®, and placebo.

Should the topline results confirm Piclidenoson's efficacy at 16 weeks as compared to placebo, we believe this would be a significant value-driving event. Piclidenoson has already been out-licensed to distribution partners in some European countries, Canada, South Korea, and China through agreements that include milestones payments, and we believe that positive results would trigger high interest in Piclidenoson in other major healthcare markets in which we are currently talking with potential partners.

Following 32 weeks of treatment, if Piclidenoson proves non-inferior to Otezla, we believe this would be a significant event in the psoriasis treatment market, as Piclidenoson and Otezla are both oral drugs in a market dominated by injection-based biologics. We believe it is Otezla's oral dosing advantage that has led to the drug capturing robust market share and being acquired by Amgen for $13 billion in 2019.

Phase IIb NASH Study Expected to Commence Patient Enrollment in Q1 2022- The study will enroll 140 patients with biopsy-confirmed NASH with a primary endpoint to evaluate the efficacy of Namodenoson as compared to placebo, as determined by a histological endpoint. Patients will be randomly assigned in a 2:1 ratio to oral doses of Namodenoson 25 mg or placebo every 12 hours for 36 weeks. There is currently no FDA approved treatment for NASH, an urgent unmet need that is a leading cause of liver transplants.

Patient Enrollment Expected to Commence in Pivotal Phase III Liver Cancer Study H1 2022– In December, we announced that a prior Phase II liver cancer study patient who continues to be treated with Namodenoson has survived five years and cleared all cancer lesions. We see this as a very positive sign as we expect to commence enrollment in the first quarter of 2022. Approximately 450 patients diagnosed with hepatocellular carcinoma (HCC) and underlying Child Pugh B7 (CPB7) who have not responded to other approved therapies will be enrolled through clinical sites worldwide. Patients will be randomized to oral treatment with either 25 mg Namodenoson or matching placebo given twice daily. The primary efficacy endpoint of the trial is overall survival. An interim analysis will be conducted by an Independent Data Monitoring Committee after 50% of patients are enrolled.

While several approved therapies exist for liver cancer, advanced patients often become unresponsive to treatment. With its liver protective properties, Namodenoson helped CPB7 patients who were unresponsive to approved treatments achieve a statistically significant improvement in overall survival as compared to placebo in our prior Phase II study. Namodenoson has been out-licensed to three partners in the indications of liver cancer and NASH in Eastern Europe, South Korea, and China.

We enter 2022 with a strong balance sheet, having raised $10 million in December in addition to the $13.3 million we reported at the end of Q3 2021. While our advanced clinical trials addressing multi-billion markets in psoriasis, liver cancer, and NASH are expected to be our main drivers, we also expect continued development and potential value events from our out-licensing of Piclidenoson to treat osteoarthritis in the veterinary market, as well as development of CF602 in the treatment of erectile dysfunction, and our preclinical work with cannabinoids.

We wish all of you a healthy and happy 2022, and we look forward to sharing significant news during the year.

Sincerely,

Pnina Fishman, Ph.D.

Chief Executive Officer

About Can-Fite BioPharma Ltd.

Can-Fite BioPharma Ltd. (NYSE American: CANF) (TASE: CFBI) is an advanced clinical stage drug development Company with a platform technology that is designed to address multi-billion dollar markets in the treatment of cancer, liver, and inflammatory disease. The Company's lead drug candidate, Piclidenoson, is currently in a Phase III trial for psoriasis. Can-Fite's liver drug, Namodenoson, is headed into a Phase III trial for hepatocellular carcinoma (HCC), the most common form of liver cancer, and a Phase IIb trial for the treatment of non-alcoholic steatohepatitis (NASH). Namodenoson has been granted Orphan Drug Designation in the U.S. and Europe and Fast Track Designation as a second line treatment for HCC by the U.S. Food and Drug Administration. Namodenoson has also shown proof of concept to potentially treat other cancers including colon, prostate, and melanoma. CF602, the Company's third drug candidate, has shown efficacy in the treatment of erectile dysfunction. These drugs have an excellent safety profile with experience in over 1,500 patients in clinical studies to date. For more information please visit: www.can-fite.com.

Forward-Looking Statements

This press release may contain forward-looking statements, about Can-Fite's expectations, beliefs or intentions regarding, among other things, market risks and uncertainties, its product development efforts, business, financial condition, results of operations, strategies or prospects. In addition, from time to time, Can-Fite or its 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 Can-Fite with the U.S. Securities and Exchange Commission, press releases or oral statements made by or with the approval of one of Can-Fite's 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 Can-Fite's actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause Can-Fite's actual activities or results to differ materially from the activities and results anticipated in 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: our history of losses and needs for additional capital to fund our operations and our inability to obtain additional capital on acceptable terms, or at all; uncertainties of cash flows and inability to meet working capital needs; the impact of the COVID-19 pandemic; 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 strategic partnerships and other 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; competitive companies, technologies and our industry; statements as to the impact of the political and security situation in Israel on our business; and risks and other risk factors detailed in Can-Fite's filings with the SEC and in its periodic filings with the TASE. In addition, Can-Fite operates in an industry sector where securities values are highly volatile and may be influenced by economic and other factors beyond its control. Can-Fite does not undertake any obligation to publicly update these forward-looking statements, whether as a result of new information, future events or otherwise.

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