

846,818,700 Ordinary Shares represented by 2,822,729 American Depositary Shares

This prospectus supplement, or the Supplement, modifies, supersedes and supplements certain information contained in, and should be read in conjunction with, that certain prospectus originally filed with the Securities and Exchange Commission, or the SEC, by Can-Fite Biopharma Ltd., the Company, dated February 10, 2023, or the Prospectus, and subsequently amended, related to the resale by the selling shareholders named therein of up to 955,909,800 ordinary shares, no par value of the Company, or ordinary shares, represented by 3,186,366 American Depository Shares, or ADSs, consisting of (i) 600,000,000 ordinary shares represented by 2,000,000 ADSs issuable upon the exercise of warrants issued in a private placement concurrently with a registered direct offering in January 2023, or the January 2023 RD Offering, at an original exercise of \$5.50 per share, or the January 2023 RD Investor Warrants, (ii) 218,182,200 ordinary shares represented by 727,274 ADSs issuable upon the exercise of warrants issued in a private placement, or the January 2023 Offerings, and (iii) 28,636,500 ordinary shares represented by 95,455 ADSs issuable upon the exercise of placement agent warrants issued in connection with the January 2023 Offerings. The currently outstanding January 2023 RD Investor Warrants, together the January 2023 Warrants, have been amended as described below under "Amendments to Existing Warrants."

The ADSs are listed on NYSE American under the symbol "CANF." On November 20, 2023, the closing price of our ADSs on the NYSE American was \$2.01 per ADS. Our ordinary shares also trade on the Tel Aviv Stock Exchange, or TASE, under the symbol "CFBI". On November 21, 2023, the last reported sale price of our ordinary shares on the TASE was NIS 2.90 or \$0.7817 per share (based on the exchange rate reported by the Bank of Israel on the same day, which was NIS 3.7100 = \$1.00).

The information contained in this Supplement modifies and supersedes, in part, the information in the Prospectus. This Supplement is not complete without, and may not be delivered or used except in connection with, the Prospectus. Any information that is modified or superseded in the Prospectus shall not be deemed to constitute a part of the Prospectus, except as modified or superseded by this Supplement.

We may amend or supplement the Prospectus from time to time by filing amendments or supplements as required. You should read the entire Prospectus and any amendments or supplements carefully before you make an investment decision. This Supplement amends only those sections of the Prospectus contained in this Supplement; all other sections of the prospectus supplement remain unchanged.

Investing in our securities involves risks. See "Risk Factors" on page 3 of the Prospectus and in the documents incorporated by reference into the Prospectus, including the risks described under "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2022.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this Supplement or the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Effective as of January 9, 2023, the ratio of our ADSs to ordinary shares changed from one (1) ADS representing thirty (30) ordinary shares to a new ratio of one (1) ADS representing three hundred (300) ordinary shares, which ratio change had the same effect as a one-for-ten reverse ADS split, or the ADS Ratio Change. All share and per share prices in this Supplement have been adjusted to reflect the ADS Ratio Change.

FORWARD-LOOKING STATEMENTS

You should carefully consider the risk factors set forth in or incorporated by reference into the Prospectus, as well as the other information contained in or incorporated by reference into this Supplement and the Prospectus. This Supplement, the Prospectus and documents incorporated therein by reference contain forward-looking statements regarding events, conditions, and financial trends that may affect our plan of operation, business strategy, operating results, and financial position. You are cautioned that any forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties. Actual results may differ materially from those included within the forward-looking statements as a result of various factors. Cautionary statements in the "Risk Factors" section of the Prospectus and the reports incorporated by reference therein identify important risks and uncertainties affecting our future, which could cause actual results to differ materially from the forward-looking statements made or included in this Supplement and the Prospectus.

AMENDMENTS TO EXISTING WARRANTS

This Supplement is being filed to disclose the following:

On November 21, 2023, the Company entered into an inducement offer letter agreement, or the Inducement Letter, with a certain holder, or the Holder, of certain of the Company's existing warrants to purchase up to (i) 1,363,637 of the Company's ADSs comprising the Series A warrants included in the January 2023 Warrants at an exercise price of \$6.00 per ADS, or the January 2023 Series A Warrants, and (ii) 600,000 of the Company's ADSs issued on December 23, 2021 at an exercise price of \$5.50 per ADS, or the December 2021 Warrants and together with the January 2023 Series A Warrants, the Existing Warrants.

Pursuant to the Inducement Letter, the Holder agreed to exercise for cash its Existing Warrants to purchase an aggregate of 1,963,637 of the Company's ADSs at a reduced exercise price of \$1.53 per ADS in consideration of the Company's agreement to issue new warrants to purchase ADSs, or the New Warrants to purchase up to an aggregate of 3,927,274 ADSs, or the New Warrant Shares, at an exercise price of \$1.75 per ADS. The Company expects to receive aggregate gross proceeds of approximately \$3.0 million from the exercise of the Existing Warrants by the Holder, before deducting placement agent fees and other offering expenses payable by the Company. In addition, the Company has agreed to reduce the exercise price of Series B warrants to purchase 1,363,637 ADSs issued in the January 2023 and held by the Holder from \$5.50 per ADS to \$1.75 per ADS and extend the term of such Series B warrants to twenty months from the Closing Date, as defined below.

The Company has also agreed to issue to H.C. Wainwright & Co., LLC, or the Placement Agent, or its designees warrants, or the Placement Agent Warrants, to purchase up to 137,455 ADSs (representing 7.0% of the Existing Warrants being exercised) which will have the same terms as the New Warrants except the Placement Agent Warrants will have an exercise price equal to \$1.9125 per share (125% of the reduced exercise price of the Existing Warrants). Similar to the New Warrants, the Placement Agent Warrants will be immediately exercisable from the date of issuance until the five year anniversary of such date.

The closing of the transactions contemplated pursuant to the Inducement Letter is expected to occur on or about November 24, 2023, or the Closing Date, subject to

satisfaction of customary closing conditions. The Company expects to use the net proceeds from these transactions for funding research and development and clinical trials and for other working capital and general corporate purposes.

No changes have been made to the other warrants issued in the January 2023 Offerings, which shares may be resold under the Prospectus, as amended by this Supplement.

The date of this Prospectus Supplement is November 21, 2023