

PROSPECTUS SUPPLEMENT
(To prospectus dated September 12, 2023)



Can-Fite BioPharma Ltd.

Up to \$2,573,000 of
American Depositary Shares Representing Ordinary Shares

This prospectus supplement amends and supplements the information in the prospectus, dated September 12, 2023, filed as a part of our registration statement on Form F-3 (File No. 333-274316), or the Registration Statement, as supplemented by our prospectus supplement, dated August 30, 2024, or collectively, the Prior Prospectus, relating to the offering, issuance and sale by us of our American Depositary Shares, or ADSs, representing our ordinary shares, no par value, from time to time that may be issued and sold under the At The Market Offering Agreement, dated August 30, 2024, or the Sales Agreement, by and between us and H.C. Wainwright & Co., LLC, or Wainwright, as sales agent, or the ATM Facility. This prospectus supplement should be read in conjunction with the Prior Prospectus, and is qualified by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the Prior Prospectus. This prospectus supplement is not complete without, and may only be delivered or utilized in connection with, the Prior Prospectus, and any future amendments or supplements thereto.

We are filing this prospectus supplement to amend the Prior Prospectus, as previously amended by the Report on Form 6-K filed by us on April 14, 2025 that reduced the maximum aggregate offering price of the ATM Facility to zero, to update the maximum amount of securities we are eligible to sell under our Registration Statement pursuant to General Instruction I.B.5 of Form F-3. As a result of these limitations and the current public float of our ordinary shares, including ordinary shares represented by ADSs, and in accordance with the terms of the Sales Agreement, we may offer and sell ADSs having an aggregate offering price of up to \$2,573,000 from time to time through Wainwright, which does not include the ADSs having an aggregate sales price of approximately \$6.1 million that were sold pursuant to the Prior Prospectus to date. In the event that we may sell additional amounts under the Sales Agreement and in accordance with General Instruction I.B.5, we will file another prospectus supplement prior to making such additional sales.

The ADSs are listed on the NYSE American under the symbol "CANF". On May 8, 2025, the closing price of the ADSs on the NYSE American was \$1.115 per ADS. Our ordinary shares also trade on the Tel Aviv Stock Exchange, or TASE, under the symbol "CANF". On May 8, 2025, the last reported sale price of our ordinary shares on the TASE was NIS 0.014 or \$0.004 per share (based on the exchange rate reported by the Bank of Israel on the same day).

We are a "foreign private issuer" under the federal securities laws and, as such, are subject to reduced public company disclosure standards for this prospectus supplement and future filings. See "Prospectus Supplement Summary—Implications of Being a Foreign Private Issuer" for additional information.

The aggregate market value of our outstanding voting and non-voting common equity held by non-affiliates as of the date of this prospectus supplement, based on the closing price of the ADSs on the NYSE American on March 18, 2025, as calculated in accordance with General Instruction I.B.5. of Form F-3, was approximately \$26 million. Pursuant to General Instruction I.B.5 of Form F-3, in no event will we sell securities in a primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75,000,000. During the prior 12 calendar month period that ends on, and includes, the date of this prospectus supplement (excluding this offering), we, we sold securities with an aggregate market value of \$6,096,953 pursuant to General Instruction I.B.5 of Form F-3. In the event that we may sell additional amounts under the Sales Agreement, we will file another prospectus supplement prior to making such additional sales.

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-4 of this prospectus supplement and on page 4 of the accompanying prospectus and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should consider before investing in our securities.

Neither the U.S. Securities and Exchange Commission, the Israel Securities Authority nor any state or other foreign securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

H.C. Wainwright & Co.

The date of this prospectus supplement is May 9, 2025