(To Prospectus dated July 28, 2025)

Up to 1,250,000 American Depositary Shares Representing 375,000,000 Ordinary Shares and accompanying 2,500,000 Common Warrants to Purchase up to 2,500,000 American Depositary Shares Representing 750,000,000 Ordinary Shares

Up to 7,083,333 Pre-Funded Warrants to Purchase up to 7,083,333 American Depositary Shares
Representing 2,124,999,900 Ordinary Shares and accompanying 14,166,666 Common Warrants to Purchase up to 14,166,666 American Depositary Shares
Representing 4,249,999,800 Ordinary Shares

Up to 583,333 Placement Agent Warrants to Purchase up to 583,333 American Depositary Shares Representing 174,999,900 Ordinary Shares

Up to 24,333,332 American Depositary Shares Representing 7,299,999,600 Ordinary Shares Issuable Upon Exercise of the Common Warrants, Pre-Funded Warrants and Placement Agent Warrants



Can-Fite Biopharma Ltd.

This prospectus supplement updates, amends and supplements the prospectus dated July 28, 2025 (as supplemented or amended from time to time, the "Prospectus"), which forms a part of our Registration Statement on Form F-1 (Registration No. 333-288890). This prospectus supplement is being filed to update and supplement the information included or incorporated by reference in the Prospectus with the information contained in our Report on Form 6-K, which was furnished to the Securities and Exchange Commission on November 21, 2025. Accordingly, we have attached the Form 6-K to this prospectus supplement. Capitalized terms used in this prospectus supplement and not otherwise defined herein have the meanings specified in the Prospectus.

This prospectus supplement is not complete without the Prospectus. This prospectus supplement should be read in conjunction with the Prospectus, which is to be delivered with this prospectus supplement, and is qualified by reference thereto, except to the extent that the information in this prospectus supplement updates or supersedes the information contained in the Prospectus. Please keep this prospectus supplement with your Prospectus for future reference.

The ADSs are listed on NYSE American under the symbol "CANF." On November 19, 2025, the closing price of our ADSs on the NYSE American was \$0.33 per ADS. Our Ordinary Shares also trade on the Tel Aviv Stock Exchange, or TASE, under the symbol "CFBI". On November 19, 2025, the sale price of our Ordinary Shares on the TASE was NIS 0.01 or \$0.00306 per share (based on the exchange rate reported by the Bank of Israel on the same day).

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page 7 of the Prospectus and other risk factors contained in the documents incorporated by reference therein, including the risks described under "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2024, for a discussion of information that should be considered in connection with an investment in our securities.

Neither the Securities and Exchange Commission, the Israeli Securities Authority nor any state securities commission has approved or disapproved of these securities or determined if the Prospectus or this prospectus supplement 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 (the "ADS Ratio Change"). All share and per share prices in this prospectus supplement have been adjusted to reflect the ADS Ratio Change.

The date of this prospectus supplement is November 21, 2025

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 November 2025

001-36203 (Commission File Number)

CAN-FITE BIOPHARMA LTD.

(Exact name of Registrant as specified in its charter)

26 Ben Gurion Street Ramat Gan 5257346 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 □

This Report of Foreign Private Issuer on Form 6-K is hereby incorporated by reference into the registrant's Registration Statements on Form S-8 (File Nos. 333-227753, 333-271384 and 333-278525) and Form F-3 (File Nos. 333-236064, 333-274316, 333-262055, 333-276000 and 333-281872), to be a part thereof from the date on which this report is submitted, to the extent not superseded by documents or reports subsequently filed or furnished.

CONTENTS

On November 18, 2025, Can-Fite BioPharma Ltd. (the "Company") entered into an agreement with the holder of warrants to purchase 16,666,666 American Depositary Shares ("ADSs") previously issued on July 29, 2025, pursuant to which in consideration for the holder's waiver of certain standstill provisions, the Company reduced the exercise price of such warrants from \$0.60 per ADS to \$0.467 per ADS.

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: November 21, 2025 By: /s/ Motti Farbstein

Motti Farbstein Chief Executive Officer and

Chief Financial Officer