

Prospectus Supplement No. 1
(To Prospectus Supplement and Prospectus dated March 31, 2025)



SENTI BIOSCIENCES HOLDINGS, INC.

Up to \$17,500,000

Common Stock

This Prospectus Supplement No. 1 (this "Supplement No. 1") to the Prospectus Supplement supplements and amends the Prospectus Supplement dated March 31, 2025 (the "ATM Prospectus Supplement") and the base prospectus dated March 31, 2025 (the "Base Prospectus") included in the Registration Statement on Form S-3 (File No. 333-285985), each filed by Senti Biosciences, Inc. (the "Predecessor Registrant") with the Securities and Exchange Commission (the "Commission") on March 20, 2025, which registration statement was declared effective with the Commission on March 31, 2025. The ATM Prospectus Supplement related to the sale of shares of the Predecessor Registrant's common stock, par value \$0.0001 per share ("Predecessor Registrant Common Stock") in accordance with the terms of a sales agreement (the "sales agreement") with Leerink Partners LLC ("Leerink Partners"), as the Predecessor Registrant's sales agent (the "sales agent"). In accordance with the terms of the sales agreement, the Predecessor Registrant may offer and sell shares of the Predecessor Registrant Common Stock having an aggregate offering price of up to \$17,500,000 from time to time through Leerink Partners, acting as the sales agent. As of the date of this Supplement No. 1, approximately \$6.0 million remained unsold pursuant to the ATM Prospectus Supplement and the sales agreement.

On April 24, 2026, Senti Biosciences Holdings, Inc., a Delaware corporation (the "Company") filed Post-Effective Amendment No. 1 to Registration Statement on Form S-3 (as so amended and supplemented, the "Registration Statement"). The Company became the successor to the Predecessor Registrant on April 24, 2026 for purposes of paragraph (d) of Rule 414 under the Securities Act of 1933, as amended, as a result of the adoption by the Predecessor Registrant of a holding company form of organizational structure (the "Reorganization") implemented in accordance with Section 251(g) of the Delaware General Corporation Law by the merger (the "Merger") of the Predecessor Registrant with Senti Biosciences Merger Sub, Inc., a Delaware corporation (the "Merger Sub") and a direct, wholly owned subsidiary of Senti Holdings, Inc., a Delaware corporation ("Senti Holdings") and a direct, wholly owned subsidiary of the Company, with the Predecessor Registrant being the surviving corporation. Upon effectiveness of the Merger, the separate corporate existence of Merger Sub ceased, and the Predecessor Registrant became a direct, wholly owned subsidiary of Senti Holdings, a direct, wholly owned subsidiary of the Company, and all shares of Predecessor Registrant Common Stock were automatically converted into shares of common stock, \$0.0001 par value ("common stock"), of the Company.

Following the consummation of the Reorganization, the Company's common stock continues to trade on the Nasdaq Capital Market (the "Nasdaq") under the ticker symbol "SENTI" with a new CUSIP number (816944 102). Immediately following the consummation of the Reorganization, on a consolidated basis, the assets, businesses, and operations of the Company are not materially different than the corresponding assets, business, and operations of the Predecessor Registrant immediately prior to the consummation of the Reorganization.

As a result of the Merger, the Company assumed the rights and obligations of the Predecessor Registrant under the sales agreement and the ATM Prospectus Supplement and Base Prospectus, as supplemented by this Supplement No. 1, relate to the offer and sale by the Company, as successor registrant to the Predecessor Registrant, pursuant to the Registration Statement of its common stock pursuant to the sales agreement.

This Supplement No. 1 is not complete without, and may not be delivered or used except in connection with, the ATM Prospectus Supplement and the Base Prospectus.

INVESTING IN THE COMPANY'S COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. BEFORE MAKING AN INVESTMENT DECISION, YOU SHOULD CAREFULLY CONSIDER ALL OF THE INFORMATION SET FORTH IN THIS PROSPECTUS SUPPLEMENT, THE ATM PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING BASE PROSPECTUS AND THE DOCUMENTS INCORPORATED BY REFERENCE THEREIN. SEE "RISK FACTORS" BEGINNING ON PAGE S-5 OF THE ATM PROSPECTUS SUPPLEMENT AND UNDER SIMILAR HEADINGS IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THE ATM PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities to be issued under this prospectus supplement or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

Leerink Partners

The date of this Supplement No. 1 is May 1, 2026.