

PROSPECTUS SUPPLEMENT
(To the Prospectus dated July 30, 2021)

\$16,415,139

Synlogic, Inc.

Common Stock

This prospectus supplement amends and supplements the information in our prospectus dated July 30, 2021 (File No. 333-258151). This prospectus supplement should be read in conjunction with the prospectus and is qualified in its entirety by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the prospectus. This prospectus supplement is not complete without, and may only be delivered or utilized in connection with, the prospectus and any future amendments or supplements thereto.

We filed the prospectus to register the offer and sale of shares of our common stock from time to time pursuant to the terms of a sales agreement, dated July 23, 2021 that we entered into with Jefferies LLC, or Jefferies, as our sales agent thereunder. As of the date of this prospectus supplement, we have sold an aggregate of 1,514,849 shares of our common stock through Jefferies under the sales agreement, resulting in net proceeds of approximately \$1.2 million. Without giving effect to any offering limit imposed by General Instruction I.B.6 of Form S-3, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time through Jefferies acting as our sales agent in accordance with the terms of the at-the-market equity offering sales agreement, including the shares of common stock that we have sold as of the date of this prospectus supplement.

On March 29, 2023, the date on which we filed our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, the prospectus became subject to the offering limits set forth in General Instruction I.B.6 of Form S-3. As of March 29, 2023, the aggregate market value of our outstanding common stock held by non-affiliates, or public float, was approximately \$49,245,416, based on 54,115,842 shares of our outstanding common stock that were held by non-affiliates on such date and a price of \$0.91 per share, which was the price at which our common stock was last sold on The Nasdaq Global Market on February 3, 2023 (a date within 60 days of the date hereof), calculated in accordance with General Instruction I.B.6 of Form S-3. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 in the 12 calendar months preceding the date of this prospectus supplement.

We are filing this prospectus supplement to amend and supplement the information in our prospectus based on the amount of securities that we are eligible to sell under General Instruction I.B.6 of Form S-3. After giving effect to the \$16,415,139 offering limit imposed by General Instruction I.B.6 of Form S-3, we may offer and sell additional shares of our common stock having an aggregate offering price of up to \$16,415,139 from time to time through Jefferies acting as our sales agent in accordance with the terms of the at-the-market equity offering sales agreement.

Our common stock is listed on The Nasdaq Global Market under the symbol "SYBX." On April 3, 2023, the last reported sale price of our common stock on The Nasdaq Global Market was \$0.58 per share.

Investing in our securities involves risks. You should read this prospectus supplement and the documents we incorporate herein by reference carefully before you make your investment decision. See "Risk Factors" set forth in the documents we file with the Securities and Exchange Commission that are incorporated by reference herein for more information.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement. Any representation to the contrary is a criminal offense.

Jefferies

Prospectus Supplement dated April 4, 2023.