

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED APRIL 15, 2021

PROSPECTUS SUPPLEMENT
(To Prospectus dated August 30, 2018)

Shares



Common Stock

We are offering _____ shares of our common stock in this offering. Our common stock is listed on The Nasdaq Capital Market under the symbol "SYBX." On April 14, 2021, the last reported sale price for our common stock on The Nasdaq Capital Market was \$3.23 per share.

Investing in our common stock involves a high degree of risk. Please read "[Risk Factors](#)" on page S-6 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus supplement or the accompanying prospectus is accurate or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions (1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have agreed to reimburse the underwriter for certain expenses. See "Underwriting."

We have granted the underwriter an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional _____ shares of our common stock. See "Underwriting" for more information.

The underwriter expects to deliver the shares of our common stock to the purchasers on or about _____, 2021.

Sole Book-Running Manager

SVB Leerink

The date of this prospectus supplement is _____, 2021.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to an offering of shares of our common stock. Before buying any shares of our common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described under the headings “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

Unless the context otherwise requires, “Synlogic,” “SYBX,” “the Company,” “we,” “us,” “our” and similar terms refer to Synlogic, Inc., a company incorporated under the laws of Delaware, together with its subsidiaries.

This document contains two parts. The first part is this prospectus supplement, which describes the terms of this offering of shares of our common stock and also adds to, updates and changes information contained in the accompanying prospectus and the documents incorporated by reference. The second part is the accompanying prospectus, which gives more general information. To the extent the information contained in this prospectus supplement differs from or conflicts with the information contained in the accompanying prospectus or any document incorporated by reference, the information in this prospectus supplement will control. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference into the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus supplement is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under the shelf registration process, we may from time to time offer and sell any combination of the securities described in the accompanying prospectus up to a total dollar amount of \$200.0 million, of which this offering is a part.

We are responsible for the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus and in any free writing prospectus we prepare or authorize. We have not, and the underwriter has not, authorized anyone to provide you with information different from that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering and we take no responsibility for any other information others may give you. We are not making, and the underwriter has not made, an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement is accurate as of the date on the front cover of this prospectus supplement only and that any information we have incorporated by reference or included in the accompanying prospectus is accurate only as of the date given in the document incorporated by reference or as of the date of the prospectus, as applicable, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus, any related free writing prospectus, or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: Neither we, nor the underwriter, has done anything that would permit this offering or possession or distribution of this prospectus supplement or the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus supplement and the accompanying prospectus.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were

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accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

All brand names or trademarks appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners. We carry on our business directly and through our subsidiaries.

Information contained on, or that can be accessed through, our website does not constitute part of this prospectus supplement, the accompanying prospectus or any related free writing prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements can generally be identified as such because the context of the statement may include words such as "may", "will", "intend", "plan", "believe", "anticipate", "expect", "estimate", "predict", "potential", "continue", "likely", "unlikely", or "opportunity", the negative of these words or words of similar import, though not all forward-looking statement contain these identifying words.

Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections incorporated by reference from our most recent Annual Report on Form 10-K. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those noted in "Risk Factors" above and those included in the documents that we incorporate by reference herein.

In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this prospectus supplement or the filing of the accompanying prospectus or documents incorporated by reference herein and therein that include forward-looking statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the factors described under the heading “Risk Factors” in this prospectus supplement and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery and development of Synthetic Biotic™ medicines. Synthetic Biotic medicines are generated from Synlogic’s proprietary drug discovery and development platform, using Synthetic Biology and leveraging a reproducible, modular approach to develop beneficial microbes that perform or deliver critical therapeutic functions. Synthetic Biotic medicines are designed to metabolize a toxic substance, compensate for missing or damaged metabolic pathways, or deliver combinations of therapeutic factors. Our goal is to discover, develop, and ultimately commercialize Synthetic Biotic medicines. Synlogic’s proprietary pipeline includes Synthetic Biotic medicines for the treatment of metabolic disorders including Phenylketonuria (PKU) and Enteric Hyperoxaluria. We are also building a portfolio of partner-able assets in immunology and oncology.

We are supported by our Board of Directors and our scientific advisory board, each of which offers complementary experience in drug discovery and development, as well as expertise in building public companies, management, and business development. Our founding science came from the laboratories of Professors James Collins and Timothy Lu from the Massachusetts Institute of Technology (MIT), who remain highly engaged in guiding development and application of our platform.

Phenylketonuria

Our co-lead metabolic product candidate is SYN1618, an oral therapy intended for the treatment of PKU, a rare metabolic disease in which an amino acid known as phenylalanine (Phe) accumulates in the body as a result of genetic defects. Elevated levels of Phe are toxic to the brain and can lead to neurological dysfunction. SYN1618 is designed to function in the gut of patients to reduce excess Phe, with the goal of lowering levels in the blood and other tissues. SYN1618 has received both Fast Track designation and orphan drug designation for PKU from the U.S. Food and Drug Administration (FDA).

We initiated a Phase 2 clinical trial with SYN1618 in the third quarter of 2020. The Phase 2 trial, referred to as the SynPheny-1 Study, is designed to evaluate safety and tolerability of a solid formulation of SYN1618 as well as its potential to lower blood Phe levels in adult PKU patients. The SynPheny-1 Study is designed to be flexible, with subjects physically coming to the clinic or participating from the patient’s home utilizing home healthcare services.

We completed a Phase 1/2a clinical trial of an early liquid formulation of SYN1618 and announced top-line data from healthy volunteers evaluated in this study in September 2018. In July 2019, we announced data that demonstrated that SYN1618 was safe and well-tolerated and achieved proof-of-mechanism of strain activity in both healthy volunteers and patients with PKU. Following the study using the liquid formulation, we developed a lyophilized formulation of SYN1618. We have evaluated this lyophilized formulation in a bridging

study in healthy volunteers. The study of this more patient- and commercialization-appropriate formulation of SYN1618 demonstrated activity and improved tolerability over the early liquid formulation. We presented this data at the American College of Medical Genetics annual meeting in April of 2021.

SYNB1618 is a member of a family of SYN1618 strains that consume Phe. We have additional Phe consuming strains for PKU in preclinical development, including SYN1934.

Enteric Hyperoxaluria

Our other co-lead metabolic product candidate is SYN8802, an oral therapy intended for the treatment of Enteric Hyperoxaluria, an acquired metabolic disorder. Enteric Hyperoxaluria is caused by increased absorption of dietary oxalate, which is present in many healthy foods such as leafy greens, nuts, and chocolate, making it difficult to control with dietary interventions. Enteric Hyperoxaluria often occurs as a result of a primary insult to the bowel, such as inflammatory bowel disease, short bowel syndrome, or surgical procedures such as Roux-en-Y bariatric weight-loss surgery. The disorder may cause dangerously high levels of urinary oxalate and progressive kidney damage, kidney stone formation, and nephrocalcinosis. There are no approved treatments.

In May 2020, we announced the nomination of a clinical candidate for Enteric Hyperoxaluria, SYN8802. We initiated a Phase 1 clinical trial of SYN8802 in the fourth quarter of 2020. This study will assess the safety, tolerability and kinetics of SYN8802 as well as the effect SYN8802 has on changes in plasma and urine biomarkers of strain activity, and the potential to reduce urinary oxalate. The study has two parts: Part A is a multiple ascending dose study in healthy volunteers in whom we will induce temporary hyperoxaluria via diet; Part B is a placebo controlled, cross-over design study in patients with Enteric Hyperoxaluria following Roux-n-Y gastric bypass surgery.

Other Metabolic Programs

We are advancing a portfolio of investigational Synthetic Biotic medicines for rare, niche, and common metabolic disorders which, similar to PKU and Enteric Hyperoxaluria, have a toxic metabolite found in the GI tract. We will disclose additional details on such programs as they move through preclinical development.

Oncology

We have also developed a portfolio of Synthetic Biotic medicines to treat certain cancers that are designed to modify the tumor microenvironment, activate the immune system and result in tumor reduction. These Synthetic Biotic medicines could be used in combination with other cancer therapies such as checkpoint inhibitors. Our first Synthetic Biotic clinical immuno-oncology (IO) candidate is SYN1891, an intratumorally administered Synthetic Biotic medicine engineered to act as a dual innate and adaptive immune activator. SYN1891 has been designed to activate the immune response in tumors via the E.coli Nissle chassis and production of cyclic di-AMP, an activator of the Stimulator of Interferon Genes, also referred to as the STING pathway. The STING pathway plays a critical role in the initiation of an anti-tumor immune response. In January 2020, we treated the first subject in a Phase 1 clinical trial of SYN1891 in patients with advanced solid tumors and lymphoma. The clinical trial is designed to identify a maximum tolerated dose (MTD) of SYN1891 delivered as a monotherapy. Once an MTD is identified, we will evaluate treatment of patients with a combination of SYN1891 and the checkpoint inhibitor atezolizumab (Tecentriq), provided through a supply agreement with Roche. Despite the COVID-19 pandemic, the Phase 1 clinical trial has remained open to both currently enrolled patients and for new patient enrollment. We released interim data from the ongoing monotherapy arm of this trial in December of 2020, which demonstrated target engagement and the production of biomarkers consistent with STING activation. In December of 2020, we also initiated the combination arm of the Phase 1 clinical trial. We provided an update on the SYN1891 Phase 1 study at the American Association for Cancer Research annual meeting in April of 2021.

Immunology

We also leverage our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases. Inflammatory bowel disease (IBD) is an attractive target for our technology as Synthetic Biotic medicines can be designed to locally deliver combinations of complementary therapeutics to potentially address the unmet medical need for maintenance of disease remissions. We have ongoing preclinical development programs in IBD, and we may enter into additional strategic partnerships in the future to maximize the value of these programs and our Synthetic Biotic platform.

Recent Updates

On March 24, 2021, we announced SYN8802, our product candidate for the treatment of Enteric Hyperoxaluria, achieved proof of mechanism in Part A of the Phase 1 dietary hyperoxaluria clinical trial in which healthy volunteers on a high oxalate and low calcium diet were treated with multiple ascending doses of SYN8802.

In the study's efficacy analysis, the percent change from baseline urinary oxalate levels were -28.6% (90% CI: -42.4 to -11.6), compared to placebo, at the 3e11 live cell dose. This dose was well tolerated and will be used in Part B of the study. We have initiated Part B of the study and will assess the urinary oxalate lowering potential of SYN8802 in patients with Enteric Hyperoxaluria following Roux-en-Y gastric bypass surgery.

Corporate Information and History

We were originally incorporated in the State of Delaware in December 2007 under the name "Mirna Therapeutics, Inc." On August 28, 2017, Mirna Therapeutics, Inc. (NASDAQ: MIRM) ("Mirna") completed its business combination with then-private Synlogic, Inc. ("Private Synlogic") in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated as of May 15, 2017, by and among Mirna, Meerkat Merger Sub, Inc. ("Merger Sub"), and Private Synlogic (the "Merger Agreement"), pursuant to which Merger Sub merged with and into Private Synlogic, with Private Synlogic surviving as a wholly owned subsidiary of Mirna (the "Merger"). On August 28, 2017, immediately after completion of the Merger, Mirna changed its name to "Synlogic, Inc." (NASDAQ: SYBX).

Our corporate headquarters are located at 301 Binney Street, Suite 402, Cambridge, Massachusetts 02142 and our telephone number is (617) 401-9975. We maintain a website at www.synlogictx.com, to which we regularly post copies of our press releases as well as additional information about us. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

The Offering

Common stock offered by us	shares
Underwriter's option to purchase additional shares	We have granted the underwriter an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to an additional shares of common stock at the public offering price less the underwriting discounts and commissions.
Common stock to be outstanding immediately after this offering	shares (or additional shares in full) shares if the underwriter exercises its option to purchase
Use of proceeds	We intend to use the net proceeds, together with our existing cash and cash equivalents, from this offering as follows: to prepare for potential entry into late phase clinical development of SYN8802; to fund process development and formulation activities as required for SYN8802, SYN1618, or other assets to advance to late stage clinical studies; to scale up manufacturing for the production of clinical material of SYN8802, SYN1618, or other assets for late stage clinical studies; to further develop pre-clinical metabolic assets and initiate IND-enabling studies; and for working capital and general corporate purposes. See "Use of Proceeds."
Risk factors	An investment in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under "Risk Factors" on page S-6 of this prospectus supplement and under similar headings in the other documents that are incorporated by reference herein and therein, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus.
Nasdaq Capital Market Symbol	Our common stock is listed on The Nasdaq Capital Market under the symbol "SYBX."

The number of shares common stock expected to be outstanding after this offering and, unless otherwise indicated, the information in this prospectus supplement are based on 38,183,273 shares of common stock outstanding as of December 31, 2020, and excludes:

- 3,343,836 shares of common stock issuable upon exercise of outstanding options as of December 31, 2020, at a weighted average exercise price of \$6.00 per share, of which 1,399,952 shares were vested as of such date;
- 636,136 shares of common stock reserved for future issuance under the 2015 Equity Incentive Award Plan;
- 575,831 shares of common stock reserved for future issuance under the 2017 Stock Incentive Plan;
- 345,662 shares of common stock reserved for future issuance under the 2015 Employee Stock Purchase Plan;

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- 2,447,211 shares of common stock issued pursuant to the Sales Agreement between Synlogic and Cowen and Company, LLC (the “Sales Agreement”) subsequent to December 31, 2020 for gross proceeds of \$8.4 million; and
- 2,548,117 shares of common stock issuable upon the exercise of pre-funded warrants held by Ginkgo Bioworks, Inc. (“Ginkgo”), exercisable at a price of \$9.00 per share, with \$8.99 of such exercise price previously paid.

Except as otherwise indicated, we have presented the information in this prospectus supplement assuming:

- no exercise by the underwriter in this offering of its option to purchase additional shares; and
- no exercise of outstanding options or warrants described above.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. Before deciding whether to invest in our common stock, you should consider carefully the risk factors discussed below and those contained in our most recent annual report on Form 10-K and our quarterly reports on Form 10-Q which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

Risks Related to this Offering

Management will have broad discretion as to the use of the net proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, and cause the price of our common stock to decline.

If you purchase shares in this offering, you will suffer immediate and substantial dilution.

If you purchase shares of our common stock in this offering, you will incur immediate and substantial dilution in the pro forma as adjusted net tangible book value of your stock of \$ _____ per share as of December 31, 2020, based on the public offering price of \$ _____ per share, because the price that you pay will be substantially greater than the net tangible book value per share of the shares you acquire. You will experience additional dilution upon the exercise of options, including those options currently outstanding and those granted in the future, and the issuance of restricted stock or other equity awards under our stock incentive plans.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of common stock or other securities convertible into or exchangeable for our shares of common stock at prices that may not be the same as the prices per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of common stock, or securities convertible or exchangeable into shares of common stock, in future transactions may be higher or lower than the prices per share paid by investors in this offering.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never paid or declared any cash dividends on our capital stock. We currently intend to retain earnings, if any, to finance the growth and development of our business and we do not anticipate paying any cash dividends in the foreseeable future. As a result, only appreciation of the price of our common stock will provide a return to our stockholders.

Sales of a substantial number of our common stock by our existing shareholders in the public market could cause our stock price to fall.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. In addition, a substantial number of shares of common stock are subject to outstanding options or will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We, our executive officers and directors have agreed that, subject to certain exceptions, during the period ending 90 days after the date of this prospectus supplement, we and they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any of our common stock or securities convertible into or exchangeable or exercisable for any of our common stock, enter into a transaction that would have the same effect, or enter into any swap or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any of these transactions are to be settled by delivery of our common stock or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of SVB Leerink LLC who may release any of the securities subject to these lock-up agreements at any time without notice. Exceptions to the lock-up restrictions are described in more detail in this prospectus supplement under the caption “Underwriting.”

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ (or approximately \$ if the underwriter's option to purchase additional shares is exercised in full) from the sale of the shares of common stock offered by us in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- to prepare for potential entry into late phase clinical development of SYN8802;
- to fund process development and formulation activities as required for SYN8802, SYN1618, or other assets to advance to late stage clinical studies;
- to scale up manufacturing for the production of clinical material of SYN8802, SYN1618, or other assets for late stage clinical studies;
- to further develop pre-clinical metabolic assets and initiate IND-enabling studies; and
- for working capital and general corporate purposes.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licensing of complementary companies, medicines or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licensing at this time, we may use a portion of the net proceeds for these purposes.

Although we currently anticipate that we will use the net proceeds from this offering as described above, there may be circumstances where a reallocation of funds is necessary. Due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. The amounts and timing of our actual expenditures will depend upon numerous factors, including the factors described under the heading "Risk Factors" in this prospectus supplement and incorporated by reference from our most recent annual report on Form 10-K. Accordingly, our management will have broad discretion in applying the net proceeds from this offering. An investor will not have the opportunity to evaluate the economic, financial or other information on which we base our decisions on how to use the proceeds.

We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We do not expect the net proceeds from this offering and our existing cash and cash equivalents to be sufficient to fund the development of our product candidates through regulatory approval and commercialization. We will need to raise substantial additional funds for further development and before we can expect to commercialize any products, if approved. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

Pending these uses, we intend to invest the net proceeds in high quality, investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or hold such proceeds as cash.

DIVIDEND POLICY

We have never paid cash dividends on any of our capital stock and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term marketable securities and capitalization as of December 31, 2020:

- on an actual basis;
- on a pro forma basis, after giving effect to the sale of 2,447,211 shares of common stock pursuant to the Sales Agreement subsequent to December 31, 2020 for gross proceeds of \$8.4 million; and
- on a pro forma as adjusted basis, giving effect to the sale of _____ shares of common stock by us in this offering for aggregate net proceeds of \$ _____ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2020		
	Actual	Pro Forma	As Adjusted
	(\$ in thousands, except share and per share data)		
Cash and cash equivalents	\$ 32,507	\$ 40,617	
Short-term marketable securities	67,937	67,937	
Shareholders' equity:			
Common stock, \$0.001 par value per share; 250,000,000 authorized; 38,183,273 issued and outstanding, actual; 40,630,484 shares issued and outstanding, pro forma; shares issued and outstanding, pro forma as adjusted	38	40	
Additional paid-in-capital	345,394	353,441	
Accumulated other comprehensive loss	14	14	
Accumulated deficit	(230,311)	(230,311)	
Total shareholders' equity	115,135	123,184	
Total capitalization	\$ 115,135	123,184	

The table above excludes:

- 3,343,836 shares of common stock issuable upon exercise of outstanding options as of December 31, 2020, at a weighted average exercise price of \$6.00 per share, of which 1,399,952 shares were vested as of such date;
- 636,136 shares of common stock reserved for future issuance under the 2015 Equity Incentive Award Plan;
- 575,831 shares of common stock reserved for future issuance under the 2017 Stock Incentive Plan;
- 345,662 shares of common stock reserved for future issuance under the 2015 Employee Stock Purchase Plan; and
- 2,548,117 shares of common stock issuable upon the exercise of pre-funded warrants held by Ginkgo exercisable at a price of \$9.00 per share, with \$8.99 of such exercise price previously paid.

DILUTION

If you invest in our common stock, your ownership interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. The net tangible book value of our common stock as of December 31, 2020 was approximately \$115.1 million, or approximately \$3.02 per share of common stock based upon 38,183,273 shares outstanding as of December 31, 2020. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding.

The pro forma net tangible book value of our common stock as of December 31, 2020 was approximately \$123.2 million, or approximately \$3.03 per share of common stock. Pro forma net tangible book value per share represents total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of December 31, 2020, after giving effect to the sale of 2,447,211 shares of common stock pursuant to the Sales Agreement subsequent to December 31, 2020 for gross proceeds of \$8.4 million.

After giving effect to the sale by us of _____ shares of common stock at the public offering price of \$ _____ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2020 would have been approximately \$ _____ million, or \$ _____ per share of common stock. This amount represents an immediate increase in pro forma as adjusted net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to purchasers in this offering. The following table illustrates the dilution:

Public offering price per share	\$
Net tangible book value per share as of December 31, 2020	\$ 3.02
Increase in net tangible book value per share attributable to pro forma adjustments	\$ 0.01
Pro forma net tangible book value as of December 31, 2020	\$ 3.03
Increase per share attributable to new investors	\$ _____
Pro forma as adjusted net tangible book value per share as of December 31, 2020, after giving effect to this offering	_____
Dilution per share to new investors purchasing shares in this offering	_____

The number of shares common stock expected to be outstanding after this offering and, unless otherwise indicated, the information in this prospectus supplement are based on 38,183,273 shares of common stock outstanding as of December 31, 2020, and excludes:

- 3,343,836 shares of common stock issuable upon exercise of outstanding options as of December 31, 2020, at a weighted average exercise price of \$6.00 per share, of which 1,399,952 shares were vested as of such date;
- 636,136 shares of common stock reserved for future issuance under the 2015 Equity Incentive Award Plan;
- 575,831 shares of common stock reserved for future issuance under the 2017 Stock Incentive Plan;
- 345,662 shares of common stock reserved for future issuance under the 2015 Employee Stock Purchase Plan; and
- 2,548,117 shares of common stock issuable upon the exercise of pre-funded warrants held by Ginkgo exercisable at a price of \$9.00 per share, with \$8.99 of such exercise price previously paid.

MATERIAL U.S. FEDERAL TAX CONSIDERATIONS

The following is a summary of the material U.S. federal income and estate tax considerations relating to the purchase, ownership and disposition of our common stock by Non-U.S. Holders (defined below). This summary does not purport to be a complete analysis of all the potential tax considerations relevant to Non-U.S. Holders of our common stock. This summary is based upon the Internal Revenue Code, the Treasury regulations promulgated or proposed thereunder and administrative and judicial interpretations thereof, all as of the date hereof and all of which are subject to change at any time, possibly on a retroactive basis.

This summary assumes that shares of our common stock are held as “capital assets” within the meaning of Section 1221 of the Internal Revenue Code (generally, property held for investment). This summary does not purport to deal with all aspects of U.S. federal income and estate taxation that might be relevant to particular Non-U.S. Holders in light of their particular investment circumstances or status, nor does it address specific tax considerations that may be relevant to particular persons (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain U.S. expatriates, tax-exempt organizations, pension plans, “controlled foreign corporations”, “passive foreign investment companies”, corporations that accumulate earnings to avoid U.S. federal income tax, persons in special situations, such as those who have elected to mark securities to market or those who hold common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment, or holders subject to the alternative minimum or the 3.8% Medicare tax on net investment income). In addition, except as explicitly addressed herein with respect to estate tax, this summary does not address estate and gift tax considerations or considerations under the tax laws of any state, local or non-U.S. jurisdiction.

For purposes of this summary, a “Non-U.S. Holder” means a beneficial owner of common stock that for U.S. federal income tax purposes is not classified as a partnership and is not:

- an individual who is a citizen or resident of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is included in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the trust’s administration and one or more U.S. persons have the authority to control all of the trust’s substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of persons treated as its partners for U.S. federal income tax purposes will generally depend upon the status of the partner and the activities of the partnership. Partnerships and other entities that are classified as partnerships for U.S. federal income tax purposes and persons holding our common stock through a partnership or other entity classified as a partnership for U.S. federal income tax purposes are urged to consult their own tax advisors.

There can be no assurance that the Internal Revenue Service (IRS) will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain a ruling from the IRS with respect to the U.S. federal income or estate tax consequences to a Non-U.S. Holder of the purchase, ownership or disposition of our common stock.

THIS SUMMARY IS FOR GENERAL INFORMATION ONLY AND IS NOT INTENDED TO BE TAX ADVICE. NON-U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS CONCERNING

THE U.S. FEDERAL INCOME AND ESTATE TAXATION, STATE, LOCAL AND NON-U.S. TAXATION AND OTHER TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK.

Distributions on our common stock

As discussed under “Dividend Policy” above, we do not currently expect to pay dividends. In the event that we do make a distribution of cash or property with respect to our common stock, any such distributions generally will constitute dividends for U.S. federal income tax purposes to the extent of our current and accumulated earnings and profits, if any, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will constitute a return of capital and will first reduce the holder’s adjusted tax basis in our common stock, but not below zero. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “—Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock”. Any such distribution would also be subject to the discussion below under the section titled “—Additional Withholding and Reporting Requirements”.

Dividends paid to a Non-U.S. Holder generally will be subject to a 30% U.S. federal withholding tax unless such Non-U.S. Holder provides us or our agent, as the case may be, with the appropriate IRS Form W-8, such as:

- IRS Form W-8BEN or W-8BEN-E (or successor form) certifying, under penalties of perjury, a reduction in withholding under an applicable income tax treaty, or
- IRS Form W-8ECI (or successor form) certifying that a dividend paid on common stock is not subject to withholding tax because it is effectively connected with a trade or business in the United States of the Non-U.S. Holder (in which case such dividend generally will be subject to regular graduated U.S. tax rates as described below).

The certification requirement described above must be provided to us or our agent prior to the payment of dividends and must be updated periodically. The certification also may require a Non-U.S. Holder that provides an IRS form or that claims treaty benefits to provide its U.S. taxpayer identification number. Special certification and other requirements apply in the case of certain Non-U.S. Holders that hold shares of our common stock through intermediaries or are pass-through entities for U.S. federal income tax purposes.

Each Non-U.S. Holder is urged to consult its own tax advisor about the specific methods for satisfying these requirements. A claim for exemption will not be valid if the person receiving the applicable form has actual knowledge or reason to know that the statements on the form are false.

If dividends are effectively connected with a trade or business in the United States of a Non-U.S. Holder (and, if required by an applicable income tax treaty, is attributable to a permanent establishment maintained by such Non-U.S. Holder in the United States), the Non-U.S. Holder, although exempt from the withholding tax described above (provided that the certifications described above are satisfied), generally will be subject to U.S. federal income tax on such dividends on a net income basis in the same manner as if it were a resident of the United States. In addition, if a Non-U.S. Holder is treated as a corporation for U.S. federal income tax purposes, the Non-U.S. Holder may be subject to an additional “branch profits tax” equal to 30% (unless reduced by an applicable income treaty) of its earnings and profits in respect of such effectively connected dividend income.

Non-U.S. Holders that do not timely provide us or our agent with the required certification, but which are eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, may obtain a refund or credit of any excess amount withheld by timely filing an appropriate claim for refund with the IRS.

Gain on sale, exchange or other taxable disposition of our common stock

Subject to the discussion below under the section titled “—Additional Withholding and Reporting Requirements”, in general, a Non-U.S. Holder will not be subject to U.S. federal income tax or withholding tax

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on gain realized upon such holder's sale, exchange or other taxable disposition of shares of our common stock unless (1) such Non-U.S. Holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition, and certain other conditions are met, (2) we are or have been a "United States real property holding corporation", as defined in the Internal Revenue Code (a USRPHC), at any time within the shorter of the five-year period preceding the disposition and the Non-U.S. Holder's holding period in the shares of our common stock, and certain other requirements are met, or (3) such gain is effectively connected with the conduct by such Non-U.S. Holder of a trade or business in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment maintained by such Non-U.S. Holder in the United States).

If the first exception applies, the Non-U.S. Holder generally will be subject to U.S. federal income tax at a rate of 30% (or at a reduced rate under an applicable income tax treaty) on the amount by which such Non-U.S. Holder's capital gains allocable to U.S. sources exceed capital losses allocable to U.S. sources during the taxable year of the disposition. If the third exception applies, the Non-U.S. Holder generally will be subject to U.S. federal income tax with respect to such gain on a net income basis in the same manner as if it were a resident of the United States and a Non-U.S. Holder that is a corporation for U.S. federal income tax purposes may also be subject to a branch profits tax with respect to any earnings and profits attributable to such gain at a rate of 30% (or at a reduced rate under an applicable income tax treaty).

Generally, a corporation is a USRPHC only if the fair market value of its U.S. real property interests (as defined in the Internal Revenue Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance in this regard, we believe that we are not, and do not anticipate becoming, a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we became a USRPHC, a Non-U.S. Holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock by reason of our status as USRPHC so long as our common stock is regularly traded on an established securities market at any time during the calendar year in which the disposition occurs and such Non-U.S. Holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our common stock at any time during the shorter of the five year period ending on the date of disposition and the holder's holding period. However, no assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Additional withholding and reporting requirements

Sections 1471 through 1474 of the Internal Revenue Code and related Treasury Regulations, together with other Treasury Department or IRS guidance issued thereunder, and intergovernmental agreements, legislation, rules and other official guidance adopted pursuant to such intergovernmental agreements (commonly referred to as "FATCA") generally will impose a U.S. federal withholding tax of 30% on payments to certain non-U.S. entities (including certain intermediaries), including dividends on our common stock and, on or after January 1, 2019, the gross proceeds from a sale or other disposition of shares of our common stock, unless such persons comply with a complicated U.S. information reporting, disclosure and certification regime. This regime requires, among other things, a broad class of persons to enter into agreements with the IRS to obtain, disclose and report information about their investors and account holders. An intergovernmental agreement between the United States and an applicable foreign country may, however, modify these requirements.

Prospective investors should consult their own tax advisors regarding the possible impact of these rules on their investment in our common stock, and the possible impact of these rules on the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of this 30% withholding tax under FATCA.

Backup withholding and information reporting

We must report annually to the IRS and to each Non-U.S. Holder the gross amount of the distributions on our common stock paid to the holder and the tax withheld, if any, with respect to the distributions. Non-U.S. Holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Internal Revenue Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Dividends paid to Non-U.S. Holders subject to the U.S. withholding tax, as described above under the section titled “—Distributions on Our Common Stock”, generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a Non-U.S. Holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a Non-U.S. Holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Prospective investors should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them, including the availability of and procedure for obtaining an exemption from backup withholding.

Copies of information returns may be made available to the tax authorities of the country in which the Non-U.S. Holder resides or, in which the Non-U.S. Holder is incorporated, under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder can be refunded or credited against the Non-U.S. Holder’s U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

U.S. federal estate tax

Common stock owned (or treated as owned) by an individual who is not a citizen or a resident of the United States (as defined for U.S. federal estate tax purposes) at the time of death will be included in the individual’s gross estate for U.S. federal estate tax purposes unless an applicable estate or other tax treaty provides otherwise, and therefore, may be subject to U.S. federal estate tax.

UNDERWRITING

SVB Leerink LLC is acting as sole underwriter, and sole book-running manager for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us shares of our common stock.

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If the underwriter defaults, the underwriting agreement provides that the underwriting agreement may be terminated.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officers' certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The underwriter has advised us that it proposes initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering of the shares, the public offering price, concession or any other term of this offering may be changed by the underwriter.

The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriter of its option to purchase additional shares of our common stock.

	<u>Per Share</u>	<u>Total</u>	
		<u>Without Option</u>	<u>With Option</u>
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$ _____. We also have agreed to reimburse the underwriter for up to \$25,000 for its FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering. The underwriter has agreed to reimburse us for certain expenses incurred by us in connection with this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriter, exercisable for 30 days after the date of this prospectus supplement, to purchase up to additional shares at the public offering price, less underwriting discounts and commissions. If the underwriter exercises this option, the underwriter will be obligated, subject to the conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to the underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus supplement without first obtaining the written consent of the underwriter. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or make any public announcement of an intention to do any of the foregoing;
- file, or demand filing of, any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of the underwriter, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions on transfers or other dispositions by holders of our outstanding securities described in the immediately preceding paragraph do not apply to:

- (i) as a *bona fide* gift or gifts;
- (ii) to any trust for the direct or indirect benefit of the holder;
- (iii) if the holder is an entity, as a distribution or other transfer by a partnership to its partners or former partners or to its members or retired members or by a corporation to its stockholders or former stockholders or to any wholly-owned subsidiary of such corporation;
- (iv) to affiliates or to any investment fund or other entity controlled or managed by the holder;
- (v) pursuant to a qualified domestic relations order or in connection with a divorce settlement;
- (vi) by will or intestate succession upon the death of the undersigned; or
- (vii) to the Company in satisfaction of any tax withholding obligation.

Each of the above excepts is subject to (1) the underwriter receiving a signed lock-up agreement for the balance of 90 day period from each donee, trustee, distributee, or transferee, as the case may be, (2) any such transfer shall not involve a disposition for value, (3) such transfers are not required to be reported with the Securities and Exchange Commission on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended and (4) the holder does not otherwise voluntarily effect any public filing or report regarding such transfers (other than a filing on a Form 5 made after the expiration of the 90 days period.

The restrictions on transfers or other dispositions by us described in the paragraph above do not apply to:

- transfers pursuant to a trading plan established pursuant to Rule 10b5-1 under the Securities Exchange Act of 1934, as amended;
- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus pursuant to stock plans disclosed in this prospectus;

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- the grant by us of any options to purchase shares of common stock or other awards granted under a stock incentive plan or stock purchase plan described in this prospectus, and the issuance by us of shares of common stock upon the exercise thereof, provided that we will cause each recipient of such grant to execute and deliver to the underwriter a lock-up agreement if such recipient has not already delivered one;
- the filing by us of any registration statement on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in this prospectus; or
- shares of common stock or other securities issued in connection with a joint venture, equipment leasing arrangement, licensing or collaboration transaction or other strategic transaction with an unaffiliated third party, provided that (x) the aggregate number of shares issued pursuant to this exception will not exceed 5% of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares to be sold in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this exception during the restricted period will enter into a lock-up agreement.

Nasdaq Capital Market Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol “SYBX.”

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit the underwriter and selling group members from bidding for and purchasing our common stock. However, the underwriter may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriter may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater number of shares than they are required to purchase in this offering. “Covered” short sales are sales made in an amount not greater than the underwriter’s option to purchase additional shares described above. The underwriter may close out any covered short position by either exercising its option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase shares through the option to purchase additional shares granted to it under the underwriting agreement described above. “Naked” short sales are sales in excess of such option. The underwriter must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriter in the open market prior to the closing of this offering.

Similar to other purchase transactions, the underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriter may conduct these transactions on the Nasdaq Capital Market, in the over-the-counter market or otherwise.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we

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nor any of the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

The underwriter may also engage in passive market making transactions in our common stock on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

In connection with this offering, the underwriter or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriter and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and certain of its affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a "Relevant State"), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of the underwriter; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation, *provided* that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the underwriter and us that it is a "qualified investor" within the meaning of Article 2(e) of the Prospectus Regulation. In the case of any

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shares being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriter has been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to the shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129 (as amended).

Notice to Prospective Investors in the United Kingdom

No shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the U.K. Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the U.K. Prospectus Regulation); or
- (c) in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000 (“FSMA”), *provided* that no such offer of the shares shall require us or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the U.K. Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression “U.K. Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the U.K. Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the “Order,” and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2) (a) to (e) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the FSMA. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons. Any person in the UK who is not a relevant person must not act on or rely upon this document or any of its contents.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the common stock being offered hereby will be passed upon by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. Goodwin Procter LLP, New York, New York is acting as counsel for the underwriter in connection with certain legal matters related to this offering.

EXPERTS

The consolidated financial statements of Synlogic, Inc. as of December 31, 2020 and 2019, and for each of the years in the two-year period ended December 31, 2020, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the common stock we are offering under this prospectus supplement and accompanying prospectus. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may obtain a copy of the registration statement, including the exhibits and schedules, as well as any documents filed by us with the SEC, from the SEC's website. Additionally, you may access our filings with the SEC through our website at www.synlogictx.com. The information on our website is not part of this prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities being offered pursuant to this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus omit certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities being offered pursuant to this prospectus supplement and the accompanying prospectus. Statements in this prospectus supplement and the accompanying prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the document incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 25, 2021;
- our Current Reports on Form 8-K, filed with the SEC on [February 10, 2021](#) and [April 14, 2021](#); and

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- the description of our common stock contained in our registration statement on [Form 8-A](#) as filed with the SEC on September 23, 2015, as updated or amended in any amendment or report filed for such purpose.

We undertake to provide without charge to each person (including any beneficial owner) who receives a copy of this prospectus supplement and the accompanying prospectus, upon written or oral request, a copy of all of the preceding documents that are incorporated by reference (other than exhibits, unless the exhibits are specifically incorporated by reference into these documents). You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number: 301 Binney Street, Suite 402, Cambridge, Massachusetts 02142, telephone number is (617) 401-9975.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

PROSPECTUS

Synlogic, Inc.
\$200,000,000
COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
PURCHASE CONTRACTS
UNITS

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$200,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock upon conversion of or exchange for the preferred stock; common stock, preferred stock or debt securities upon the exercise of warrants or rights; or any combination of our equity securities upon the performance of purchase contracts.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled “Plan of Distribution” in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on The Nasdaq Capital Market under the symbol “SYBX.” On August 22, 2018, the last reported sale price of our common stock was \$7.91 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Capital Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption “[Risk Factors](#).” We may include specific risk factors in supplements to this prospectus under the caption “Risk Factors.” This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

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

The date of this prospectus is August 30, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, or purchase contracts to purchase our equity securities, either individually or in units, in one or more offerings, with a total value of up to \$200,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading “Where You Can Find More Information” before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, “Synlogic,” “SYBX,” “the Company,” “we,” “us,” “our” and similar terms refer to Synlogic, Inc. and our subsidiaries.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Explanatory Note

On August 28, 2017, Synlogic, Inc., formerly known as Mirna Therapeutics, Inc., completed its business combination with what was then known as Synlogic, Inc., or Private Synlogic, in accordance with the terms of the Agreement and Plan of Merger and Reorganization, or Merger Agreement, dated as of May 15, 2017, by and among the Company, Meerkat Merger Sub, Inc., or Merger Sub, and Private Synlogic, pursuant to which Merger Sub merged with and into Private Synlogic, with Private Synlogic surviving as a wholly owned subsidiary of the Company.

About Synlogic, Inc.

Synlogic is a clinical-stage biopharmaceutical company focused on advancing drug discovery and development platform for Synthetic Biotic™ medicines, which are designed using synthetic biology to genetically reprogram beneficial microbes to treat metabolic and inflammatory diseases and cancer. Synthetic Biotic medicines are generated from Synlogic's proprietary drug discovery and development platform, applying the principles and tools of synthetic biology to engineer beneficial probiotic bacteria to perform or deliver critical therapeutic functions. As living medicines, Synthetic Biotic medicines can be designed to sense a local disease context within a patient's body and to respond by metabolizing a toxic substance, compensating for missing or damaged metabolic pathways in patients, or by delivering combinations of therapeutic factors. Synlogic's goal is to lead in the discovery and development of Synthetic Biotic therapies as living medicines capable of robust and precise pathway complementation and delivery of therapeutic benefit.

Additional Information

For additional information related to our business and operations, please refer to the reports incorporated herein by reference, as described under the caption "Incorporation of Documents by Reference" on page 29 of this prospectus.

Our Corporate Information

We were originally incorporated in the State of Delaware in December 2007 under the name "Mirna Therapeutics, Inc." As used herein, the words "Synlogic," "SYBX," the "Company," "we," "us," and "our" refer to Synlogic, Inc. and our subsidiaries.

Our corporate headquarters are located at 301 Binney St., Suite 402, Cambridge, Massachusetts 02142 and our telephone number is (617) 401-9975. We maintain a website at www.synlogictx.com, to which we regularly post copies of our press releases as well as additional information about us. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

All brand names or trademarks appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

Offerings Under This Prospectus

Under this prospectus, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, or purchase contracts to purchase our equity securities, either individually or in units, with a total value of up to \$200,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any; and
- conversion or exercise prices, if any.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

RISK FACTORS

Investing in our securities involves significant risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in Synlogic. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” included in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K that we have filed with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and incorporated by reference in this prospectus, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The sections in our periodic reports, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, entitled “Business,” “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” as well as other sections in this prospectus and the documents or reports incorporated by reference in this prospectus, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- the success of our research and development efforts;
- the initiation, progress, timing, costs and results of clinical trials for our product candidates;
- the time and costs involved in obtaining regulatory approvals for our product candidates;
- the progress, timing, and costs involved in developing manufacturing processes and agreements with third-party manufacturers;
- the rate of progress and cost of our commercialization activities;
- the success of our research and development efforts;
- the expenses we incur in marketing and selling our product candidates;
- the revenue generated by sales of our product candidates;
- the emergence of competing or complementary technological developments;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish;
- the acquisition of businesses, products and technologies;
- our need to implement additional infrastructure and internal systems; and
- our need to add personnel and financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this prospectus or in the documents incorporated by reference

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in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. For a summary of such factors, please refer to the section entitled “Risk Factors” in this prospectus, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in any supplements to this prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus to fund activities relating to the advancement of our drug discovery and development programs, and for other general corporate purposes, including, but not limited to, working capital, capital expenditures, investments, acquisitions, should we choose to pursue any, and collaborations. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade, interest-bearing securities or apply them to the reduction of short-term indebtedness.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed from time to time;
- market prices prevailing at the time of sale;
- prices related to the prevailing market prices; or
- negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time, and may enter into arrangements for “at-the-market,” equity line or similar transactions. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in each applicable prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

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- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

One or more firms, referred to as “remarketing firms,” may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm’s compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters’ commissions, discounts or concessions may qualify as underwriters’ compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority, Inc., or FINRA.

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for listing and trading on The Nasdaq Capital Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Capital Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of or the existence, development or maintenance of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

DESCRIPTION OF COMMON STOCK

We are authorized to issue 250,000,000 shares of common stock, par value \$0.001 per share. As of August 22, 2018, we had 25,430,948 shares of common stock outstanding and approximately 138 stockholders of record.

The following summary of certain provisions of our common stock does not purport to be complete. You should refer to the section of this prospectus entitled “Certain Provisions of Delaware Law and of the Company’s Certificate of Incorporation and Bylaws” and our amended and restated certificate of incorporation, as amended, or the restated certificate of incorporation, and our amended and restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future. All shares of common stock outstanding as of the date of this prospectus and, upon issuance and sale, all shares of common stock that we may offer pursuant to this prospectus, will be fully paid and nonassessable.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. There are no redemption or sinking fund provisions applicable to the common stock. Our outstanding shares of common stock are validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC, with offices at 6201 15th Avenue, Brooklyn, New York 11219.

Stock Exchange Listing

Our common stock is listed for quotation on The Nasdaq Capital Market under the symbol “SYBX.”

DESCRIPTION OF PREFERRED STOCK

The following description of preferred stock and the description of the terms of any particular series of preferred stock that Synlogic chooses to issue hereunder are not complete. These descriptions are qualified in their entirety by reference to Synlogic's restated certificate of incorporation and the certificate of designation relating to any series of preferred stock issued by Synlogic. The rights, preferences, privileges and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to that series.

Synlogic currently has no shares of Synlogic's preferred stock outstanding. The Synlogic Board of Directors has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions granted to or imposed upon the preferred stock. Any or all of these rights may be greater than the rights of the Synlogic common stock.

The Synlogic Board of Directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could negatively affect the voting power and other rights of the holders of Synlogic common stock. Preferred stock could thus be issued quickly with terms calculated to delay or prevent a change in control of Synlogic or make it more difficult to remove Synlogic's management. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of Synlogic common stock.

The Synlogic Board of Directors may specify the following characteristics of any preferred stock:

- the maximum number of shares;
- the designation of the shares;
- the annual dividend rate, if any, whether the dividend rate is fixed or variable, the date or dates on which dividends will accrue, the dividend payment dates, and whether dividends will be cumulative;
- the price and the terms and conditions for redemption, if any, including redemption at the option of Synlogic or at the option of the holders, including the time period for redemption, and any accumulated dividends or premiums;
- the liquidation preference, if any, and any accumulated dividends upon the liquidation, dissolution or winding up of Synlogic's affairs;
- any sinking fund or similar provision, and, if so, the terms and provisions relating to the purpose and operation of the fund;
- the terms and conditions, if any, for conversion or exchange of shares of any other class or classes of Synlogic's capital stock or any series of any other class or classes, or of any other series of the same class, or any other securities or assets, including the price or the rate of conversion or exchange and the method, if any, of adjustment;
- the voting rights;
- any or all other preferences and relative, participating, optional or other special rights, privileges or qualifications, limitations or restrictions; and
- any preferred stock issued will be fully paid and nonassessable upon issuance.

Transfer Agent and Registrar

The transfer agent and registrar for our preferred stock will be set forth in the applicable prospectus supplement.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part. We use the term “indentures” to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term “debenture trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- the title or designation;
- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place or places where payments will be payable;

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- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;
- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion of any material or special U.S. federal income tax considerations applicable to a series of debt securities;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;

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- if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

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- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; *provided, however*, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

- the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants may be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock, warrants or purchase contracts, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights. We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether stockholders are entitled to oversubscription rights, if any;
- any applicable material U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any

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other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts for the purchase or sale of equity securities issued by us.

Each purchase contract will entitle the holder thereof to purchase or sell, and obligate us to sell or purchase, on specified dates, such equity securities issued by us at a specified purchase price, which may be based on a formula, as set forth in the applicable prospectus supplement. The applicable prospectus supplement will also specify the methods by which the holders may purchase or sell such securities and any acceleration, cancellation or termination provisions or other provisions relating to the settlement of a purchase contract.

Any purchase contracts we issue will be physically settled by delivery of the securities. The purchase contracts may require the holders thereof to secure their obligations in a specified manner to be described in the applicable prospectus supplement. Alternatively, purchase contracts may require holders to satisfy their obligations thereunder when the purchase contracts are issued. Our obligation to settle such pre-paid purchase contracts on the relevant settlement date may constitute indebtedness.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, one or more debt securities, warrants or rights for the purchase of common stock, preferred stock and/or debt securities in one or more series, or purchase contracts to purchase our equity securities, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under “Description of Common Stock,” “Description of Preferred Stock,” “Description of Debt Securities,” “Description of Warrants,” “Description of Rights” and “Description of Purchase Contracts” will apply to each unit, as applicable, and to any common stock, preferred stock, debt security, warrant, right or purchase contract included in each unit, as applicable.

Unit Agent

The name and address of the unit agent, if any, for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act

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as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

**CERTAIN PROVISIONS OF DELAWARE LAW AND
OF THE COMPANY'S CERTIFICATE OF INCORPORATION AND BYLAWS**

Anti-Takeover Provisions

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Charter Documents

Our restated certificate of incorporation and amended and restated bylaws divide our board of directors into three classes with staggered three year terms. The provision for a classified board could prevent a party who acquires control of a majority of Synlogic's outstanding voting stock from obtaining control of the Synlogic Board of Directors until the second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. Synlogic's classified board provision could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of Synlogic and could increase the likelihood that incumbent directors will retain their positions. Synlogic's restated certificate of incorporation provides that, subject to the special rights of holders of one or more series of preferred stock, directors may be removed at any time, but only for cause by the affirmative vote of the holders of at least 66 and 2/3% of the voting power of all outstanding voting stock of Synlogic.

Synlogic's restated certificate of incorporation provides that certain amendments of Synlogic's certificate of incorporation and amendments by Synlogic stockholders of Synlogic's amended and restated bylaws require the approval of at least 66 and 2/3% of the voting power of all outstanding stock. These provisions could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of Synlogic and could delay changes in management.

Synlogic's amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of Synlogic stockholders, including proposed nominations of persons for election to the Synlogic Board of Directors. At an annual meeting, stockholders may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the Synlogic Board of Directors. Stockholders may also consider a proposal or nomination by a person who was a stockholder at the time of giving notice and at the time of the meeting, who is entitled to vote at the meeting and who has complied with the notice requirements of Synlogic's amended and restated bylaws in all respects provided that such proposal is properly made in accordance with Rule 14a-8 under the Exchange Act. The amended and restated bylaws do not give the Synlogic Board of Directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting of the stockholders. However, Synlogic's amended and restated bylaws may have the effect of precluding the conduct of business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the potential acquirer's own slate of directors or otherwise attempting to obtain control of Synlogic.

Synlogic's amended and restated bylaws provide that a special meeting of Synlogic stockholders may be called at any time by the Synlogic Board of Directors. Because Synlogic stockholders do not have the right to call a

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special meeting, a Synlogic stockholder cannot force stockholder consideration of a proposal over the opposition of the Synlogic Board of Directors by calling a special meeting of stockholders prior to such time as a majority of the Synlogic Board of Directors believed the matter should be considered and such Synlogic stockholder would only be able to force consideration of such proposal at the next annual meeting, *provided* that the requestor met the notice requirements. The restriction on the ability of Synlogic stockholders to call a special meeting means that a proposal to replace one or more directors on the Synlogic Board of Directors also could be delayed until the next annual meeting.

Synlogic's amended and restated bylaws do not allow stockholders to act by written consent without a meeting. Without the availability of stockholder action by written consent, a holder controlling a majority of Synlogic's capital stock would not be able to amend Synlogic's amended and restated bylaws or remove directors without holding a stockholders' meeting.

Limitation of Liability and Indemnification

Synlogic's restated certificate of incorporation contains provisions that limit the liability of Synlogic's directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, Synlogic's directors will not be personally liable to Synlogic or Synlogic stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to Synlogic or Synlogic stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the DGCL; or
- any transaction from which the director derived an improper personal benefit.

Synlogic's restated certificate of incorporation and amended and restated bylaws provide that Synlogic is required to indemnify its directors and officers, in each case to the fullest extent permitted by Delaware law. The amended and restated bylaws also provide that Synlogic is obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit Synlogic to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether Synlogic would otherwise be permitted to indemnify him or her under Delaware law.

Synlogic has entered and expects to continue to enter into agreements to indemnify its directors, executive officers and other employees as determined by the Synlogic Board of Directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding brought against them by reason of the fact that they are or were Synlogic's agents. Synlogic believes that these provisions in Synlogic's restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified directors and officers. Synlogic also maintains directors' and officers' liability insurance. This description of the limitation of liability and indemnification provisions of Synlogic's restated certificate of incorporation, amended and restated bylaws and indemnification agreements is qualified in its entirety by reference to these documents.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities to be offered by this prospectus.

EXPERTS

The consolidated financial statements of Synlogic, Inc. as of December 31, 2017 and 2016, and for each of the years in the two-year period ended December 31, 2017, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at <http://www.sec.gov>. This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at www.synlogictx.com, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2017 that we filed with the SEC on March 20, 2018;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018 and June 30, 2018 that we filed with the SEC on [May 15, 2018](#) and [August 9, 2018](#), respectively;
- our Current Reports on Form 8-K that we filed with the SEC on [January 24, 2018](#), [April 6, 2018](#), [June 6, 2018](#) and [June 13, 2018](#) (except for the information furnished under Items 2.02 or 7.01 and the exhibits furnished thereto);
- the description of our common stock contained in our Registration Statement on [Form 8-A](#) initially filed on September 23, 2015, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

The SEC file number for each of the documents listed above is 001-37566.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting:

Synlogic, Inc.
301 Binney St., Suite 402
Cambridge, Massachusetts 02142
Attention: Investor Relations
Telephone: (617) 401-9975

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You may also access these documents on our website, [http:// www.synlogictx.com](http://www.synlogictx.com). The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

Shares



Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

SVB Leerink

, 2021
