Filed Pursuant to Rule 424(b)(5)
Registration No. 333-220948

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 JANUARY 23, 2018

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated October 25, 2017)

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 January 22, 2018, the last reported sale price for our common stock on the Nasdaq Capital Market was $10.63 per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements.

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 underwriters for certain expenses. See "Underwriting."

We have granted the underwriters 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.

Certain of our existing stockholders, who are affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $15 million in shares of common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares of common stock in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, fewer or no shares of common stock in this offering.

The underwriters expect to deliver the shares of our common stock to the purchasers on or about , 2018.

Joint Book-Running Managers

Leerink Partners **Piper Jaffray**

Lead Manager

H.C. Wainwright & Co.

The date of this prospectus supplement is , 2018.

Table of Contents

PROSPECTUS SUPPLEMENT

PROSPECTUS

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 underwriters have 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, and the underwriters are not, making 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 underwriters, have 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 accompany 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 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.

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 and our Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC. 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 advancing our 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 our proprietary drug discovery and development platform. We apply the principles and tools of synthetic biology to engineer beneficial probiotic bacteria to perform or deliver critical therapeutic functions such as compensating for missing or damaged metabolic pathways in patients. 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 or delivering combinations of therapeutic factors.

Our initial focus is on metabolic diseases with the potential to be corrected following oral delivery of a living medicine to the gut. This includes a group of rare genetic diseases called inborn errors of metabolism ("IEMs"), as well as acquired metabolic diseases caused by organ dysfunction. Our approach to selecting these initial programs is based on the potential of the Synthetic Biotic platform to uniquely address conditions in which there is (1) unmet medical need with (2) well understood biology that is (3) based on an imbalance of a metabolite and (4) where that metabolite is available within or originating from the gut lumen. Additional considerations include the availability of animal models, relevant biomarkers and feasible clinical development paths. Our initial clinical and preclinical programs are focused on certain IEMs that share these characteristics. When delivered orally, Synthetic Biotic medicines are designed to act from the gut to compensate for the dysfunctional metabolic pathway with the intended consequence of reducing the systemic levels of the toxic metabolites. We believe that success in IEMs will enable us to demonstrate the potential of our oral Synthetic Biotic medicines to address metabolic dysfunction while bringing meaningful change to the lives of patients suffering from these debilitating conditions.

Our two lead therapeutic programs are being developed for the treatment of hyperammonemia and phenylketonuria ("PKU"). There are unmet needs to improve current therapies for both indications and opportunities to reduce toxic metabolites that originate from the gut. Both also inform the potential of the Synthetic Biotic platform in unique ways. Our lead Synthetic Biotic program is SYNB1020. SYNB1020 is an oral therapy intended for the treatment of patients with hyperammonemia. In patients with these conditions ammonia accumulates in the body and becomes toxic leading to neurocognitive crisis and risk of long-term cognitive or behavioral impairment, coma or death. Hyperammonemic conditions include urea cycle disorders ("UCD") and hepatic encephalopathy ("HE") in patients with liver disease. SYNB1020 has received both Fast Track Designation and orphan drug designation for UCD from the U.S. Food and Drug Administration (the "FDA"). We initiated a Phase 1 clinical trial in June 2017 to evaluate the safety and tolerability of SYNB1020 in healthy volunteers. In November 2017, we announced top-line data from this study that demonstrated that SYNB1020 was safe and well-tolerated and achieved proof-of-mechanism. In 2018, we intend to initiate two Phase 1b / 2a studies for SYNB1020 in patients with elevated blood ammonia.

Our second program, SYNB1618, is an oral therapy intended for the treatment of PKU, in which the amino acid 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. SYNB1618 is designed to have activity in the gut of patients to reduce excess circulating Phe, resulting in normalization of levels in the blood and tissues. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. We are planning to initiate a Phase 1 / 2a clinical trial for SYNB1618 in the first half of 2018.

Our early-stage metabolic pipeline includes discovery-stage product candidates for additional IEMs, including maple syrup urine disease (“MSUD”), isovaleric acidemia (“IVA”) and organic acidemias. These are rare metabolic deficiencies in which the toxic accumulation of metabolites such as branched chain amino acids in the case of MSUD can lead to neurological decline and death. There are no currently approved pharmaceutical therapies for these disorders, ultimately resulting in patients relying on liver transplants when possible. We believe that developing therapies for this group of rare diseases will demonstrate the potential of our oral Synthetic Biotic medicines to address metabolic dysfunction, while bringing meaningful change to lives of patients suffering from these debilitating conditions. In addition, we are leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including acquired metabolic diseases, inflammation and cancer. We have established a collaboration with Ginkgo Bioworks, a privately held synthetic biology company, to discover new living medicines to treat neurological and liver disorders. We also have a collaboration with AbbVie S.à.r.l. (“AbbVie”) to develop Synthetic Biotic medicines for the treatment of inflammatory bowel disease (“IBD”).

Recent Developments

Positive Phase 1 Clinical Results for SYNB1020

In November 2017, we announced positive top-line data from our Phase 1 clinical trial of SYNB1020 commenced in June 2017. The trial successfully met its primary objectives, demonstrating safety and tolerability in healthy volunteers and identifying the maximum tolerated dose. SYNB1020 did not colonize and was cleared within the expected timeframe in subjects who had completed follow-up. Viability and evidence of mechanistic activity of the Synthetic Biotic was demonstrated in feces of subjects who received SYNB1020, but not in control subjects. Furthermore, in the multiple ascending dose component of the Phase 1 trial, daily dosing of SYNB1020 over 14 days in healthy volunteers enabled identification of a dose-response relationship between SYNB1020 oral administration and changes in a nitrogen endpoint in plasma which was found to be statistically significant in the highest dose cohort compared to placebo.

Orphan Drug Designation for SYNB1618

In October 2017, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to SYNB1618, our preclinical-stage drug candidate for the treatment of phenylketonuria (PKU), an inborn error of metabolism (IEM) caused by a mutation in the gene that breaks down the amino acid phenylalanine (Phe). The Orphan Drug Act provides for granting special status to a drug or biological product intended to treat a rare disease or condition affecting fewer than 200,000 people in the U.S. upon request of a sponsor. The designation provides development and commercial incentives for designated compounds and medicines, including eligibility for a seven-year period of market exclusivity in the U.S. after product approval, FDA assistance in clinical trial design and an exemption from FDA user fees.

Financial Update

As of December 31, 2017, we had cash, cash equivalents and marketable securities of approximately $87.0 million.

The estimated cash, cash equivalents, and marketable securities as of December 31, 2017 are preliminary and may change, are based on information available to management as of the date of this prospectus supplement, and are subject to completion by management of the financial statements as of and for the year ended December 31, 2017. There can be no assurance that our cash, cash equivalents, and marketable securities as of December 31, 2017 will not differ from these estimates, including as a result of quarter-end closing and any such changes could be material.

The foregoing preliminary financial data has been prepared by, and is the responsibility of, our management. This data could change as a result of further review. Complete annual results will be included in our Annual Report on Form 10-K for the year ended December 31, 2017.

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: MIRN) (“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 200 Sidney Street, Cambridge, Massachusetts 02139 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. We carry on our business directly and through our subsidiaries. As used herein, the words “Synlogic,” “SYBX,” the “Company,” “we,” “us,” and “our” refer to Synlogic, Inc. and our subsidiaries. Our subsidiary Synlogic Operating Company, Inc. was incorporated in Delaware as TMC Therapeutics, Inc. on March 14, 2014.

The Offering

Common stock offered by us	shares
Underwriters' option to purchase additional shares	We have granted the underwriters 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 shares if the underwriters exercise their option to purchase additional shares in full)
Use of proceeds	We intend to use the net proceeds, together with our existing cash and cash equivalents, from this offering as follows: to fund our two planned Phase 1b / 2a clinical trials of SYNB1020 (one study involving HE patients and the other study involving UCD patients) through completion; to fund activities in process development, formulation and toxicology as needed for subsequent initiation of a Phase 2b clinical trial in patients with liver cirrhosis with elevated blood ammonia; to fund our planned Phase 1 / 2a clinical trial of SYNB1618 through completion and to support acceleration of a Phase 2b clinical trial of SYNB1618 for PKU patients and continued process development and formulation activities; to fund further preclinical development in our immuno-oncology programs and drug discovery activities in our other programs; 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-4 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 16,284,885 shares of common stock outstanding as of September 30, 2017, and excludes:

- 841,510 shares issuable upon the exercise of options outstanding as of September 30, 2017 at a weighted average exercise price of $14.65 per share;
- 48,863 shares reserved for issuance under the Synlogic, Inc. 2017 Stock Incentive Plan; and
- 450,389 shares reserved for issuance under the Synlogic, Inc. 2015 Equity Incentive Award Plan.

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

- no exercise by the underwriters in this offering of their option to purchase additional shares; and
- no exercise of outstanding options and no vesting and restricted stock units described above.

Certain of our existing stockholders, who are affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $15 million in shares of common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares of common stock in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, fewer or no shares of common stock in this offering.

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 quarterly report on Form 10-Q which is on file with the SEC and is 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 as adjusted net tangible book value of your stock of $ per share as of September 30, 2017, 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, as well as upon the vesting of outstanding restricted stock units, 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 are 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 and certain of our existing shareholders 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 Leerink Partners LLC and Piper Jaffray & Co., 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.”

Risks Related to Our Financial Condition, Capital Requirements and Operating Results

We are a clinical-stage biopharmaceutical company with a history of losses, and we expect to continue to incur losses for the foreseeable future, and we may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company focused on the development of Synthetic Biotics and we have incurred significant operating losses since our inception in 2014. Our net loss was approximately $21.0 million and $8.5 million for the fiscal years ended December 31, 2016 and 2015, respectively, and approximately $28.7 million for the nine months ended September 30, 2017. As of September 30, 2017, we had an accumulated deficit of approximately $60.0 million. To date, we have not generated any product revenue. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We have no products on the market and have initiated clinical development for only one product candidate, SYNB1020, and expect that it will be many years, if ever, before we have a product candidate ready for commercialization.

We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials, the regulatory review process for product candidates, and the development of manufacturing and marketing capabilities for any product candidates approved for commercial sale. The amount of our potential future losses is uncertain. To achieve profitability, we must successfully develop product candidates, obtain regulatory approvals to market and commercialize product candidates, manufacture any approved product candidates on commercially reasonable terms, establish a sales and marketing organization or suitable third-party alternatives for any approved product candidates and raise sufficient funds to finance our business activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in our value could also cause our stockholders to lose all or part of their investment.

We will require substantial additional funding, which may not be available on acceptable terms, or at all.

We have used substantial funds to discover and develop our programs and proprietary drug development platform and will require substantial additional funds to conduct further research and development, including

preclinical studies and clinical trials of our product candidates, seek regulatory approvals for our product candidates and manufacture and market any products that are approved for commercial sale. We expect that the capital resources available to us as of September 30, 2017 will be sufficient to meet our anticipated cash requirements for at least the next 12 months. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing research and development and corporate activities. Because we cannot be certain of the length of time or activities associated with successful development and commercialization of our product candidates, we are unable to estimate the actual funds we will require to develop and commercialize them.

We do not expect to realize any appreciable revenue from product sales or royalties in the foreseeable future, if at all. Our revenue sources will remain very limited unless and until our product candidates complete clinical development and are approved for commercialization and successfully marketed. To date, we have primarily financed our operations through sales of our securities, our third-party collaborations and our merger with Mirna. We intend to seek additional funding in the future through collaborations, equity or debt financings, credit or loan facilities or a combination of one or more of these financing sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity or convertible debt securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets.

If we are unable to obtain funding on a timely basis or on acceptable terms, or at all, we may have to delay, limit or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our product candidates or technologies that we would otherwise pursue on our own.

Our quarterly and annual operating results may fluctuate in the future. As a result, we may fail to meet the expectations of research analysts or investors, which could cause our stock price to decline.

Our financial condition and operating results may fluctuate from quarter to quarter and year to year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following factors, as well as factors described elsewhere in this prospectus supplement and others:

- our ability to achieve or maintain profitability;
- our ability to develop and maintain Synthetic Biotic technologies;
- our ability to manage our growth;
- the outcomes of research programs, clinical trials, or other product development and approval processes;
- our ability to accurately report our financial results in a timely manner;
- our dependence on, and the need to attract and retain, key management and other personnel;
- our ability to obtain, protect and enforce our intellectual property rights;
- our ability to prevent the theft or misappropriation of our intellectual property, know-how or technologies;

- potential advantages that our competitors and potential competitors may have in securing funding or developing competing technologies or products; and
- our ability to obtain additional capital that may be necessary to expand our business.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

Our stock price is volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, such as reports by industry analysts, investor perceptions or negative announcements by other companies involving similar technologies or diseases. These factors also include those discussed in this "Risk Factors" section of this prospectus supplement and others such as:

- announcements relating to collaborations that we may enter into with respect to the development or commercialization of our product candidates;
- announcements relating to the receipt, modification or termination of government contracts or grants;
- termination or delay of a development program;
- product liability claims related to our clinical trials or product candidates;
- prevailing economic conditions;
- additions or departures of key personnel;
- business disruptions caused by earthquakes or other natural disasters;
- disputes concerning our intellectual property or other proprietary rights;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- sales of our common stock by the company, our executive officers and directors or our stockholders in the future;
- future sales or issuances of equity or debt securities by us;
- lack of an active, liquid and orderly market in our common stock;
- fluctuations in our quarterly operating results; and
- the issuance of new or changed securities analysts' reports or recommendations regarding us.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that have been often unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

Our short operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We commenced active operations in 2014. Our operations to date have been limited to organizing and staffing our company, research

and development activities, business planning and raising capital. In June 2017, we initiated a Phase 1 clinical trial with SYNB1020, however all of our other therapeutic programs are still in the preclinical development stage. We will need to transition from a company with a research focus to a company capable of supporting clinical development and commercial activities. In addition, we expect to initiate a Phase 1 / 2a clinical trial of SYNB1618 in the first half of 2018. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes many years to develop one new product candidate from the time it is discovered to the time that it becomes available for treating patients. We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may hinder our success in commercializing one or more of our product candidates. Further, drug development is a capital-intensive and highly speculative undertaking that involves a substantial degree of risk. You should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development and clinical trials. Any forward-looking statements regarding our future prospects, plans or viability may not be as accurate as they may be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Risks Related to the Development of Our Product Candidates

Clinical trials are costly, time consuming and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Clinical development of a product candidate is expensive, time consuming and involves significant risk. We cannot guarantee that any clinical trials we undertake to conduct will be conducted as planned or completed on schedule or at all. A failure of one or more clinical trials can occur at any stage of development. Events that may prevent successful or timely completion of clinical development of our product candidates include but are not limited to:

- inability to generate satisfactory preclinical or other nonclinical data, including, toxicology, or other in vivo or in vitro data or diagnostics to support the initiation or continuation of clinical trials;
- delays in reaching agreement on acceptable terms with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in obtaining required institutional review board approval at each clinical trial site;
- failure to permit the conduct of a clinical trial by regulatory authorities, after review of an investigational new drug or equivalent foreign application or amendment;
- delays in recruiting qualified patients in our clinical trials;
- failure by clinical sites or CROs or other third parties to adhere to clinical trial requirements;
- failure by us, clinical sites, CROs or other third parties to perform in accordance with the good clinical practices requirements of the FDA or applicable foreign regulatory guidelines;
- patients dropping out of the clinical trials;
- occurrence of adverse events, unacceptable side effects or toxicity issues associated with our product candidates;
- imposition by the FDA of a clinical hold or the requirement by other similar regulatory agencies that one or more clinical trials be delayed or halted;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or performing additional nonclinical studies;
- the ultimate affordability of the cost of clinical trials of our product candidates;

- negative or inconclusive results from our clinical trials that may result in us deciding, or regulators requiring us, to conduct additional clinical trials or abandon such clinical trials and/or clinical trials or development programs in other ongoing or planned indications for a product candidate; and
- delays in reaching agreement on acceptable terms with third-party manufacturers or delays or failure in manufacturing sufficient quantities of our product candidates for use in clinical trials.

Any inability to successfully complete clinical development and obtain regulatory approval for our product candidates could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional preclinical studies or the results obtained from such new formulation may not be consistent with previous results obtained. Clinical trial delays could also shorten any anticipated periods of patent exclusivity for our product candidates and may allow competitors to develop and bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

The approach we are taking to discover and develop novel therapeutics using synthetic biology to create novel medicines is unproven and may never lead to marketable products.

The scientific discoveries that form the basis for our efforts to generate and develop our product candidates are relatively recent. The scientific evidence to support the feasibility of developing drugs based on our approach is both preliminary and limited. Synthetic Biotics represent a novel therapeutic modality and their successful development by us may require additional studies and efforts to optimize their therapeutic potential. Any product candidates that we develop may not demonstrate in patients the therapeutic properties ascribed to them in laboratory and other preclinical studies, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways. If we are not able to successfully develop and commercialize product candidates based upon this technological approach, we may never become profitable and the value of our capital stock may decline.

Our Synthetic Biotic product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

We have concentrated our research and development efforts to date on a limited number of product candidates based on our Synthetic Biotic therapeutic platform and identifying our initial targeted disease indications. Our future success depends on our successful development of viable product candidates. There can be no assurance that we will not experience problems or delays in developing our product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved.

The clinical trial and manufacturing requirements of the FDA, the European Medicines Agency and other regulatory authorities, and the criteria these regulators use to determine the safety and efficacy of a product candidate, vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. The regulatory approval process for novel product candidates such as Synthetic Biotic therapeutics may be more expensive and take longer than for other, better known or more extensively studied therapeutic modalities. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates, even if approved for marketing. Approvals by the European Medicines Agency or national regulatory agencies may not be indicative of what the FDA, and vice versa, may require for approval and different or additional preclinical studies or clinical trials may be required to support regulatory approval in each respective jurisdiction. In addition, the FDA has advised us that the clinical development of SYNB1020 does not require submission to the National Institutes of Health's ("NIH") Recombinant DNA Advisory Committee ("RAC"), a committee that reviews human gene transfer protocols. Nevertheless, if RAC review is deemed necessary by one or more of our clinical trial sites that receives NIH funding, our clinical trials could be delayed. Our product candidates do not involve gene transfers to humans, and we believe that they do not meet any of the criteria for that type of review. Delay or failure to obtain, or

unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

We may not be successful in our efforts to use and expand our development platform to build a pipeline of product candidates.

A key element of our strategy is to use our targeted focus and experienced management and scientific team to create Synthetic Biotic medicines that can be deployed against a broad range of human disease in order to build a pipeline of product candidates. Although our research and development efforts to date have resulted in potential product candidates, we may not be able to continue to identify and develop additional product candidates. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, these potential product candidates may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position. There is no assurance that we will be successful in our preclinical and clinical development, and the process of obtaining regulatory approvals will, in any event, require the expenditure of substantial time and financial resources.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or terminate our clinical trials or result in a restrictive label or delay regulatory approval by the FDA or comparable foreign authorities. Undesirable side effects and negative results for other indications may negatively impact the development and potential for approval of our product candidates for their proposed indications.

Additionally, even if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of or revoke licenses for such products;
- regulatory authorities may require additional warnings on the labels of such products;
- we may be required to create a risk evaluation and mitigation strategy (“REMS”) plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, even if approved, and could significantly harm our business, results of operations, and prospects.

Our product development program may not uncover all possible adverse events that patients who take our product candidates may experience. The number of subjects exposed to our product candidates during clinical trials and the average exposure time in the clinical development program may be inadequate to detect rare adverse events, or chance findings, that may only be detected once the product is administered to more patients and for greater periods of time.

Clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of patients and limited duration of exposure, we cannot be fully assured that uncommon or severe side effects of

our product candidates will be uncovered. Such side effects may only be uncovered with a significantly larger number of patients exposed to the drug. If such safety problems occur or are identified after a product candidate reaches the market, the FDA may require that we amend the labeling of the product or recall the product, or may even withdraw approval for the product. Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, even if approved, and could significantly harm our business, results of operations, and prospects.

We are heavily dependent on the success of our product candidates. Some of our product candidates have produced results in preclinical settings to date, but none of our product candidates have completed all required clinical trials, and we cannot give any assurance that we will generate data for any of our product candidates sufficient to receive regulatory approval in our planned indications, which will be required before they can be commercialized.

We have invested substantially all of our efforts and financial resources to identify, acquire and develop our portfolio of product candidates. Our future success is dependent on our ability to successfully further develop, obtain regulatory approval for, and commercialize one or more product candidates. We currently generate no revenue from sales of any products, and we may never be able to develop or commercialize a product candidate.

In addition, only our lead product candidate has advanced into clinical trials, and none of our product candidates has advanced into any pivotal clinical trial, for our proposed indications and it may be years before any additional clinical trials, including any pivotal clinical trial, are initiated and completed, if at all. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. We cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

If we fail to obtain or maintain orphan drug exclusivity for some of our products, our competitors may obtain approval to sell competing drugs to treat the same conditions and our revenues will be reduced.

As part of our business strategy, we have developed and may in the future develop product candidates that may be eligible for FDA and European Commission orphan drug designation. In August 2016, the FDA granted orphan drug designation to SYNB1020 for the treatment of UCD and in October 2017, the FDA granted orphan drug designation to SYNB1618 for the treatment of PKU. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat, diagnose or prevent rare diseases or conditions that affect fewer than 200,000 people in the United States. In the EU, orphan drug designation may be granted to drugs intended to treat, diagnose or prevent a life-threatening or chronically debilitating disease having a prevalence of no more than five in 10,000 people in the EU. The company that first obtains FDA approval for a designated orphan drug for the associated rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost under several circumstances, including a later determination by the FDA that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. Similar regulations are in effect in the EU with a ten-year period of market exclusivity.

Because the extent and scope of patent protection for some of our product candidates is limited, obtaining orphan drug designation is especially important for any product candidates that may be eligible for orphan drug designation. For eligible products, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug designation for our product candidates that do not have broad patent protection, our competitors may then seek to sell a competing drug to treat the same condition and our revenues, if any, may be adversely affected thereby.

Even though we have obtained orphan drug designation for certain of our product candidates, and intend to seek orphan drug designation for other product candidates, there is no assurance that we will be the first to obtain marketing approval for any particular rare indication. Further, even though we have obtained orphan drug designation for certain of our product candidates, or even if we obtain orphan drug designation for other potential product candidates, such designation may not effectively protect us from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions and potentially used off-label in the orphan indication. Even after an orphan drug is approved, the FDA can subsequently approve a competing drug for the same condition for several reasons, including, if the FDA concludes that the later drug is safer or more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.

The results from preclinical studies or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in later stage clinical trials of that product candidate or any other product candidate. Flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and we may be unable to design and execute clinical trials to support regulatory approval of our product candidates. In addition, preclinical study and clinical trial data are often susceptible to varying interpretations and analyses. Product candidates that seemingly perform satisfactorily in preclinical studies and clinical trials may nonetheless fail to obtain regulatory approval. There is a high failure rate for drugs proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could negatively affect our business and operating results.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Clinical trials of a new product candidate require the enrollment of a sufficient number of patients suffering from the disease or condition the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the potential patient population, the age and condition of the patients, the stage and severity of disease or condition, the nature and requirements of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease or condition, the perceived risks, benefits and convenience of administration of the product candidate being studied, the patient referral practices of physicians, our efforts to facilitate timely enrollment in clinical trials, and the eligibility criteria for the clinical trial. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments, can result in increased costs, longer development times or termination of a clinical trial.

In addition, our success may depend, in part, on our ability to identify patients who qualify for our clinical trials, or are likely to benefit from any product candidate that we may develop, which will require those potential patients to undergo a screening assay for the presence or absence of a particular genetic sequence or clinical trait. Genetically defined diseases generally, and especially those for which our current product candidates are targeted, may have relatively low prevalence. For example, we estimate there are approximately 2,000 patients diagnosed with UCD in the United States, and approximately 16,500 patients that may be diagnosed with PKU in the United States. If we, or any third parties that we engage to assist us, are unable to successfully identify patients with these diseases, or experience delays in doing so, then we may not realize the full commercial potential of any product candidate we develop.

We may face potential product liability claims, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use or misuse of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals, if any, could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. If we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, such liability could adversely affect our financial condition.

The use or misuse of our product candidates in clinical trials and the sale of any products for which we may obtain marketing approval exposes us to the risk of potential product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates and approved products, if any. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. Patients with the diseases targeted by our product candidates may already be in severe and advanced stages of disease and have both known and unknown significant preexisting and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which an adverse event is unrelated to our product candidates, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may delay our regulatory approval process or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

Although we have product liability insurance, which covers any clinical trial we may conduct in the United States, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer. We will also likely be required to increase our product liability insurance coverage for the advanced clinical trials that we plan to initiate. If we obtain marketing approval for any of our product candidates, we will need to expand our insurance coverage to include the sale of commercial products. There is no way to know if we will be able to continue to obtain product liability coverage and obtain expanded coverage we may require, in sufficient amounts to protect us against losses due to liability, on acceptable terms, or at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites or limitations on approved indications;
- the inability to commercialize, or if commercialized, decreased demand for, our product candidates;
- if commercialized, product recalls, withdrawals of labeling, marketing or promotional restrictions or the need for product modification;
- initiation of investigations by regulators;
- loss of revenues;
- substantial costs of litigation, including monetary awards to patients or other claimants;

- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business; and
- damage to our reputation and the reputation of our products and our technology.

Product liability claims may subject us to the foregoing and other risks, which could have a material adverse effect on our business, financial condition or results of operations.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

We may seek breakthrough therapy designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a breakthrough therapy designation from the FDA for some of our product candidates. A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs or biological products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA could also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify and are designated as breakthrough therapies, the FDA may later decide that the drugs or biological products no longer meet the conditions for designation and the designation may be rescinded.

We may seek Fast-Track designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not actually lead to a faster development or regulatory review or approval process.

If a product candidate is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for the condition, a product sponsor may apply for FDA Fast-Track designation. We were awarded Fast-Track designation for SYNB1020 in June 2017. Fast-Track designation does not ensure that we will receive marketing approval for the product candidate or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with Fast-Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast-Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast-Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Even if we obtain regulatory approval for a product candidate, we will remain subject to ongoing regulatory requirements.

If any of our product candidates are approved for marketing, we will be subject to ongoing regulatory requirements, including with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing clinical trials, and submission of safety, efficacy and other post-approval information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices ("cGMP") regulations and corresponding foreign regulatory manufacturing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any Biologic License Application ("BLA") or marketing authorization application.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product candidate may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. We will be required to report adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. If our original marketing approval for a product candidate was obtained through an accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial in order to confirm the clinical benefit for our products. An unsuccessful post-marketing clinical trial or failure to complete such a trial could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval or revoke a license;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- require a product recall.

Any government investigation of alleged violations of law would be expected to require us to expend significant time and resources in response and could generate adverse publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and our value and operating results would be adversely affected.

Healthcare legislative reform measures may have a material adverse effect on our financial condition or results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health

Care and Education Reconciliation Act (collectively, the "ACA"), was passed, which was intended to substantially change the way health care is financed by both governmental health programs and private insurers, and significantly impact the U.S. pharmaceutical industry. The ACA, among other things, introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of specified branded prescription drugs, and promotes a new Medicare Part D coverage gap discount program.

The ACA has been under scrutiny by the U.S. Congress almost since its passage, and certain sections of the ACA have not been fully implemented or effectively repealed. As a result, its longevity continues to be uncertain. In addition, ongoing initiatives in the U.S. have increased and will continue to increase pressure on drug pricing. The announcement or adoption of any such initiative could have an adverse effect on potential revenues from any product candidate that we may successfully develop.

It is anticipated that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been judicial and Congressional challenges to certain aspects of the ACA, and it is expected there will be additional challenges and amendments to the ACA in the future, especially with the recent change in administration. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes specified requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the ACA require manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human

Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including governmental and private payors, to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business, financial condition or results of operations.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our research and development efforts, commercialization efforts and business operations and environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of specified materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Given the nature of the research and development work conducted by us, we do not currently carry biological or hazardous waste insurance coverage.

Laws and regulations governing international operations may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop, implement and maintain costly compliance programs.

To develop, manufacture and sell certain products outside the United States, we must dedicate resources to comply with numerous laws and regulations in each jurisdiction in which we operate. The Foreign Corrupt Practices Act ("FCPA"), prohibits any United States individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees may be considered government employees or foreign officials. In other circumstances, certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-United States nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. These laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions and export control laws.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of preclinical or clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Ethical, legal and social concerns about synthetic biology and genetic engineering could limit or prevent the use of our technologies and limit our revenues.

Our technologies involve the use of synthetic biology and genetic engineering. Public perception about the safety and environmental hazards of, and ethical concerns over, synthetic biology and genetic engineering could influence public acceptance of our technologies, product candidates and processes. If we and our collaborators

are not able to overcome the ethical, legal and social concerns relating to synthetic biology and genetic engineering, our technologies, product candidates and processes may not be accepted. These concerns could result in increased expenses, regulatory scrutiny and increased regulation, trade restrictions on imports of Synthetic Biotic medicines, delays or other impediments to our programs or the public acceptance and commercialization of Synthetic Biotic medicines. Further, there is a risk that Synthetic Biotic medicines made using our technologies could result in adverse health effects or other adverse events, which could also lead to negative publicity. We design and produce product candidates with characteristics comparable or disadvantaged to those found in naturally occurring organisms or enzymes in a controlled laboratory; however, the release of such organisms into uncontrolled environments could have unintended consequences. Any adverse effect resulting from such a release could have a material adverse effect on our business, financial condition or results of operations and we may have exposure to liability for any resulting harm.

Risks Related to Our Intellectual Property

We may not be successful in obtaining or maintaining necessary rights to Synthetic Biotic targets, product candidates and processes for our development pipeline through acquisitions and in-licenses.

Presently, we have rights to certain intellectual property, through licenses from third parties and under patents and patent applications owned by us. The growth of our business will likely depend in part on our ability to obtain, maintain or enforce our and our licensors' intellectual property rights and to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates or delivery systems that may require the use of additional proprietary rights held by third parties. Our ultimate product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations.

In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by other third parties. We may be unable to develop, acquire or in-license compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of other companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These companies could have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we have previously and may continue to collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to it. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

We intend to rely on patent rights and the status of our product candidates, if approved, as biologics eligible for exclusivity under the Biologics Price Competition and Innovation Act (BPCIA). If Synlogic is unable to obtain or maintain exclusivity from the combination of these approaches, Synlogic may not be able to compete effectively in our markets.

We rely or will rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large

part on our and our licensors' ability to obtain regulatory exclusivity and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Even if we cannot obtain and maintain effective protection of exclusivity from our regulatory efforts and intellectual property rights, including patent protection, data exclusivity or orphan drug exclusivity, for our product candidates, we believe that our product candidates will be protected by exclusivity that prevents approval of a biosimilar in the United States for a period of twelve years from the time the product to which it claims similarity was first approved. However, The Biologics Price Competition and Innovation Act of 2009, Title VII, Subtitle A of the Patent Protection and Affordable Care Act, Pub.L.No.111-148, 124 Stat.119, Sections 7001-02 signed into law March 23, 2010, and codified in 42 U.S.C. §262 (the "BPCIA"), created an elaborate and complex patent dispute resolution mechanism for biosimilars that could prevent us from launching our product candidates in the United States or could substantially delay such launches. Current biosimilars litigation are addressing certain requirements of the BPCIA which is creating uncertainty over how certain terms of the BPCIA should be construed and this, presents uncertainty for both the biologics innovator and biosimilar party. The BPCIA mechanism required for biosimilar applicants may pose greater risk that patent infringement litigation will disrupt our activities and add increased expenses as well as divert management's attention. If a biosimilar version of one of our product candidates were approved in the United States, it could have a negative effect on our business.

We may not have sufficient patent term protections for our product candidates to effectively protect our business.

Patents have a limited term. In the United States, the statutory expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a

product candidate, we may be open to competition. In addition, upon issuance in the United States any patent term can be adjusted based on specified delays caused by the applicant(s) or the USPTO.

Patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent or data exclusivity terms of our product candidates. We will likely seek patent term extensions, and we cannot provide any assurances that any such patent term extensions will be obtained and, if so, for how long. As a result, we may not be able to maintain exclusivity for our product candidates for an extended period after regulatory approval, if any, which would negatively impact our business, financial condition, results of operations and prospects. If we do not have sufficient patent terms or regulatory exclusivity to protect our product candidates, our business and results of operations will be adversely affected.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products, and recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biotechnology companies, our success is heavily dependent on patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in specified circumstances and weakened the rights of patent owners in specified situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our proposed markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent. We also utilize processes for which patents are difficult to enforce. In addition, other elements of our products, and many elements of our product candidate discovery and development processes involve proprietary know-how, information or technology that is not covered by patents. Trade secrets may be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, collaborators, advisors, independent contractors or other third parties. We also seek to preserve the integrity and confidentiality of our data and trade secrets, including by maintaining physical and electronic security of our premises and our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, collaborators, advisors, independent contractors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot

provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business, financial condition or results of operations. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technology without infringing the patent rights of third parties. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the area of Synthetic Biotics. We are aware of U.S. and foreign patents and pending patent applications owned by third parties that cover similar therapeutic uses as the product candidates we are developing. We are currently monitoring these patents and patent applications. We may in the future pursue available proceedings in the U.S. and foreign patent offices to challenge the validity of these patents and patent applications. In addition, or alternatively, we may consider whether to seek to negotiate a license of rights to technology covered by one or more of such patents and patent applications. If any patents or patent applications cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned, absent such a license, which may not be available to us on commercially reasonable terms, or at all.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patents may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to specified limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

There have been many lawsuits and other proceedings filed by third parties involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination, post-grant review and equivalent proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We depend, in part, on our licensors to file, prosecute, maintain, defend and enforce patents and patent applications that are material to our business.

While we normally seek and gain the right to fully prosecute the patent applications relating to our product candidates, there may be times when the patent applications enabling our product candidates are controlled by our licensors. If any of our existing or future licensors fail to appropriately and broadly prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, importing, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors in effect from actions prior to us assuming control over patent prosecution.

If we fail to comply with obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to certain intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing agreements impose, and we expect that future license agreements will impose, certain obligations, including the payment of milestones and royalties based on revenues from sales of our products utilizing the technologies licensed from our licensors, and such obligations could adversely affect the overall profitability for us of any products that we may seek to commercialize. In addition, we will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our product candidates covered under our license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our third-party licensors. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, these agreements may be subject to termination by the licensor which could have a material adverse effect on our business.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we or one of our licensing partners may be required to file patent infringement claims against a third party to enforce one of our patents which can be expensive, time-consuming and unpredictable. In addition, in an infringement proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, clarity or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or other jurisdictions, even outside the context of litigation. Such mechanisms include

re-examination, inter partes review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or unenforceability, we may lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions or correct inventorship with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation, derivation or interference proceedings may result in a decision adverse to our interests and, even if successful, may result in substantial costs and distract our management and other employees. In addition, we may be unable to raise the funds necessary to conduct our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. Any disclosure of confidential information could adversely affect our business. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may in the future be subject to claims that former employees, consultants, collaborators, advisors, independent contractors or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). Therefore, our rights to these patents may not be exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, co-owners from whom we do not yet have a license or assignment may raise claims surrounding inventorship or ownership of patents that ultimately issue from this patent family, potentially resulting in issued patents to which we would not have rights under our existing license agreements. Further, in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. In addition, we may have inventorship disputes arising from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship of our patents. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims that our employees, consultants, collaborators, advisors, independent contractors or other third parties have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at universities, academic research institutions and at other biotechnology or

pharmaceutical companies, including our competitors or potential competitors. Although we have written agreements with and makes every effort to ensure that our employees, consultants, collaborators, advisors, independent contractors or other third parties do not use the proprietary information or intellectual property rights of others in their work for us, we may in the future be subject to claims that our employees, consultants, collaborators, advisors, independent contractors or other third parties have inadvertently or intentionally used or disclosed confidential information of these third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States can have a different scope and strength and be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties (including competitors) from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but where enforcement rights are not as strong as those in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries, particularly some developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patents and other intellectual property rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing and could provoke third parties to assert claims of infringement or misappropriation against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have filed for trademark registration of certain marks relating to our current branding. If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners

of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Our Reliance on Third Parties

We rely, and expect to continue to rely, on third parties to conduct some aspects of our product formulation, research, preclinical, and clinical studies, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such formulation, research or testing.

We do not independently conduct all aspects of our drug discovery activities, compound formulation research or preclinical studies of product candidates. We currently rely, and expect to continue to rely, on third parties to conduct some aspects of our research and development and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our studies that support our clinical trial applications and our clinical trials are conducted in accordance with the study plan and protocols for the trial. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for clinical trial application submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

We rely on third-party supply and manufacturing partners for drug supplies for our research and development, preclinical activities, and clinical activities, and may do the same for any commercial supplies of our product candidates.

We rely on third-party supply and manufacturing partners to supply the materials and components for, and manufacture, a portion of our research and development and preclinical study drug supplies and may do the same for any clinical trial drug supplies. We have not yet manufactured or formulated any product candidate on a commercial scale and may not be able to do so for any of our product candidates. We will work to develop and optimize our manufacturing process, and we cannot be sure that the process will result in therapies that are safe, potent or effective.

We do not own manufacturing facilities or supply sources for such components and materials, but may develop these capabilities in the future. There can be no assurance that our supply of research and development, preclinical and clinical development drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of any product formulation manufacturer we may engage could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP regulations. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform our obligations to us in relation to quality, timing or otherwise, or if our supply of components or

other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We may rely on third party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;
- subjecting our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreement. With respect to our collaboration agreements, we indemnify our collaborators from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consulting agreements, we indemnify consultants from claims arising from the good faith performance of their services.

Should our obligation under an indemnification provision exceed applicable insurance coverage or should we be denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we may be exposed to risks related to those collaborations and alliances.

We are currently party to an agreement with AbbVie. Biotechnology companies sometimes become dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of product candidates. If we elect to enter into collaborative arrangements or strategic alliances, these arrangements may place the development of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Dependence on collaborative arrangements or strategic alliances would subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the relevant product candidates;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights, such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete our obligations under any arrangement;
- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and
- collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

We may attempt to form collaborations in the future with respect to our product candidates, but we may not be able to do so, which may cause us to alter our development and commercialization plans.

We may attempt to form strategic collaborations, create joint ventures or enter into licensing arrangements with third parties with respect to our programs or platform that we believe will complement or augment our existing business. We may face significant competition in seeking appropriate strategic collaborators, and the negotiation process to secure appropriate terms is time consuming and complex. We may not be successful in our efforts to establish such a strategic collaboration for any product candidates and programs on terms that are acceptable to us, or at all. This may be because our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, the competitive or intellectual property landscape may be viewed as too intense or risky, and/or third parties may not view our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile.

Any delays in identifying suitable collaborators and entering into agreements to develop and/or commercialize our product candidates could delay the development or commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Absent a strategic collaborator, we would need to undertake development and/or commercialization activities at our own expense. If we elect to fund and undertake development and/or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our product candidates or bring them to market and our business may be materially and adversely affected.

If we commit certain material breaches under our agreement with the Gates Foundation, and fail to cure them, the Gates Foundation may exercise a right to obtain a license to certain of our intellectual property or require us to redeem shares of our Capital Stock held by the Gates Foundation and our affiliates.

In September 2014, we entered into a letter agreement with the Bill & Melinda Gates Foundation (the "Gates Foundation"). In connection with the agreement, the Gates Foundation purchased $1.0 million of Series A-1

preferred stock, $1.4 million of Series A-2 preferred stock and $2.6 million of Class A-3 preferred units, and we committed to use a portion of the investment by the Gates Foundation to generally develop our Synthetic Biotic platform for potential use in neglected diseases prioritized by the Gates Foundation. In the event the Gates Foundation terminates the agreement for certain specified uncured material breaches by us, we will be obligated, among other remedies, to redeem the securities purchased by the Gates Foundation or to facilitate the purchase of such securities by a third party (in certain circumstances, We may instead satisfy such obligation by registering the resale of the securities into the public markets or through the ability of the Gates Foundation to resell the securities without volume limitations in reliance on Rule 144 under the Securities Act), and/or the Gates Foundation may exercise its right to obtain a non-exclusive license to certain of our intellectual property for use in certain prioritized diseases in developing countries. Additionally, in the six months following such sale or redemption, if we engage in certain specified corporate transactions that would value the sold or redeemed shares at more than 200% of the valuation used for the sale or redemption, we will be required to compensate the Gates Foundation for the difference between what the Gates Foundation would have received and what it actually received under the sale or redemption. If we instead elect to register the resale of the securities into the public markets or the Gates Foundation resells the securities in reliance on Rule 144, we will be required to compensate the Gates Foundation for the difference between what the Gates Foundation initially invested and what it actually received under such resale if there is any shortfall. If we are required to redeem such shares or to compensate the Gates Foundation following a specified corporate transaction or a resale, our financial condition could be materially and adversely affected. If the Gates Foundation exercises its right to obtain a non-exclusive license and develops and commercializes product candidates and products that we are also developing and commercializing, such exercise could have an adverse impact on our market position.

Risks Related to Commercialization of Our Product Candidates

If any of our product candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future products.

We currently have no sales, marketing or distribution capabilities or experience. If any of our product candidates is approved for marketing and commercialization, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved for marketing and commercialization in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects may be adversely affected.

If the market opportunities for our product candidates are smaller than we believe they are, we may not meet our revenue expectations and, assuming approval of a product candidate, our business may suffer. Because the patient populations in the market for our product candidates may be small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

Given the small number of patients who have the diseases that we are targeting, our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our product candidates. Our

projections of both the number of people who have applicable diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our business, financial condition, results of operations and prospects.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The development and commercialization of new products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to our product candidates that we may seek to develop or commercialize in the future. For example, Horizon Pharma plc, Dimension Therapeutics, Inc. (currently in definitive agreement for acquisition by Ultragenyx Pharmaceutical Inc.), Aeglea BioTherapeutics, Inc., Arcturus Therapeutics Inc., Castle Creek Pharma LLC, PhaseRx, Inc., Translate Bio (formerly Rana Therapeutics) and Selecta Biosciences, Inc. have developed or are developing product candidates for the treatment of UCD; Valeant Pharmaceuticals International, Inc., Ocera Therapeutics, Inc. (recently acquired by Mallinckrodt Pharmaceuticals), Umecrine Cognition AB, Salix Pharmaceuticals, Ltd, as well as other preclinical and discovery stage companies have developed or are each developing product candidates for the treatment of HE; and BioMarin, Inc., MipSalus ApS, Dimension Therapeutics, Inc. and Synthetic Biologics, Inc. have developed or are developing product candidates for the treatment of PKU. Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective or less costly than the product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

In addition to the competition we face from alternative therapies for the diseases we intend to target with our product candidates, we are also aware of several companies that are also working specifically to develop engineered bacteria as cellular drug therapies, such as Intrexon Corp. Further there are several companies working to develop other similar products. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Third-party payors, including governmental and private insurers, may also encourage the use of generic products.

If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Failure of our product candidates to effectively compete against established treatment options or in the future with new products currently in development would harm our business, financial condition, results of operations and prospects.

The commercial success of any of our current or future product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our products will depend in part on the health care providers, patients, and third-party payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients and third-party payors. The degree of market acceptance of any of our products will depend on a number of factors, including but not limited to:

- the efficacy of the product as demonstrated in clinical trials and potential advantages over competing treatments;
- the safety and side effect profile of the product as demonstrated in clinical trials and potential advantages over competing treatments;
- the prevalence and severity of the disease targeted;
- the clinical indications for which approval is granted, including any limitations or warnings contained in a product's approved labeling;
- the convenience and ease of administration;
- the cost of treatment;
- the willingness of the patients and physicians to accept products engineered from bacteria and these therapies;
- the perceived ratio of risk and benefit of these therapies by physicians, patients, and payers, and the willingness of physicians to recommend these therapies to patients based on such risks and benefits;
- the marketing, sales and distribution support for the product;
- the publicity concerning the products or competing products and treatments; and
- the pricing and availability of third-party insurance coverage and reimbursement.

Even if a product displays a favorable efficacy and safety profile upon approval, market acceptance of the product remains uncertain. Efforts to educate the medical community and third-party payors on the benefits of the products may require significant investment and resources and may never be successful. If our products fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and other health care providers, we will not be able to generate sufficient revenue to become or remain profitable.

We may not be successful in any efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business is also expected to depend in part upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;

- our product candidates may not succeed in preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during development or commercialization so that such a product may become unreasonable to continue to develop or commercialize;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors.

If any of these events occur, we may be forced to abandon our development efforts for one or more product candidates, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business, financial condition or results of operations and could potentially cause us to cease operations.

Failure to obtain or maintain adequate reimbursement or insurance coverage for products, if any, could limit our ability to market those products and decrease our ability to generate revenue.

The pricing, coverage, and reimbursement of our approved products, if any, must be sufficient to support our commercial efforts and other development programs and the availability and adequacy of coverage and reimbursement by third-party payors, including governmental and private insurers, are essential for most patients to be able to afford expensive treatments. Sales of our approved products, if any, will depend substantially, both domestically and abroad, on the extent to which the costs of our approved products, if any, will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide products for free or we may not be able to successfully commercialize our products.

In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates such as ours and what reimbursement codes our product candidates may receive if approved.

Outside the United States, international operations are generally subject to extensive governmental price controls and other price-restrictive regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of products. In many countries, the prices of products are subject to varying price control mechanisms as part of national health systems. Price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products, if any. Accordingly, in markets outside the United States, the potential revenue from the sale of our products may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products

and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with products due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs has and is expected to continue to increase in the future. As a result, profitability of our products, if any, may be more difficult to achieve even if they receive regulatory approval.

Risks Related to Our Business Operations and Employees

Our failure to attract and retain senior management and key scientific personnel may prevent us from successfully developing our product candidates or any future product candidate, conducting our clinical trials and commercializing any products.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We believe that our future success is highly dependent upon the contributions of our senior management, particularly our president and chief executive officer, chief financial officer, chief medical officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of the products we develop.

Although we have not historically experienced significant difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all.

Our employees, independent contractors, principal investigators, CROs, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, consultants and collaborators may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (1) regulations of regulatory authorities in jurisdictions where we are performing activities in relation to our product candidates, including those laws requiring the reporting of true, complete and accurate information to such authorities; (2) manufacturing regulations and standards; (3) fraud and abuse and anti-corruption laws and regulations; or (4) laws that require the reporting of true and accurate financial information and data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, bias, misconduct, kickbacks, self-dealing and other abusive practices, and these laws may differ substantially from country to country. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting ourselves from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending itself or asserting our rights, those actions could have a significant impact on our business including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in subsidized healthcare programs in a given country, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to the Our Common Stock

Our common stock may be delisted from the Nasdaq Capital Market if we are unable to maintain compliance with Nasdaq's continued listing standards.

Nasdaq imposes, among other requirements, continued listing standards including minimum bid and public float requirements. The price of our common stock must trade at or above $1.00 to comply with Nasdaq's minimum bid requirement for continued listing on the Nasdaq Capital Market. If our stock trades at bid prices of less than $1.00 for a period in excess of 30 consecutive business days, Nasdaq could send a deficiency notice to the company for not remaining in compliance with the minimum bid listing standards. During the third quarter of fiscal year 2017, our common stock never traded below $1.00. However, if the closing bid price of our common stock fails to meet Nasdaq's minimum closing bid price requirement, or if we otherwise fail to meet any other applicable requirements of Nasdaq and we are unable to regain compliance, Nasdaq may make a determination to delist our common stock.

Any delisting of our common stock could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease. Furthermore, if our common stock were delisted it could adversely affect our ability to obtain financing for the continuation of our operations and/or result in the loss of confidence by investors, customers, suppliers and employees.

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of September 30, 2017, our executive officers and directors, together with holders of 5% or more of our common stock outstanding and their respective affiliates, beneficially own approximately 57% of our common stock. Accordingly, these stockholders have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of the company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, Section 102 of the JOBS Act also provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. An "emerging growth company" can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. However, we are choosing to "opt out" of such extended transition period, and as a result, we will comply with new or revised

accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.

If our existing stockholders or holders of our options 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. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of September 30, 2017, there were a total of 16,284,921 shares of our common stock outstanding.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of our operating expenses;
- receipt, modification or termination of government contracts or grants, and the timing of payments we receive under these arrangements;
- Our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make under these arrangements; and
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of the company's stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Provisions of our charter documents or Delaware law could delay or prevent an acquisition of us, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for you to change management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our Board of Directors. These provisions include:

- a classified board of directors so that not all directors are elected at one time;
- a prohibition on stockholder action through written consent;
- no cumulative voting in the election of directors;
- the exclusive right of our Board of Directors to elect a director to fill a vacancy created by the expansion of our Board of Directors or the resignation, death or removal of a director;
- a requirement that special meetings of our Stockholders be called only by our Board of Directors, the chairman of our Board of Directors, the chief executive officer or, in the absence of a chief executive officer, the president;

- an advance notice requirement for stockholder proposals and nominations;
- the authority of our Board of Directors to issue preferred stock with such terms as our Board of Directors may determine; and
- a requirement of approval of not less than 66 2/3% of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation.

In addition, Delaware law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% or more of the company's voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Delaware law may discourage, delay or prevent a change in control of the company. Furthermore, our amended and restated certificate of incorporation specifies that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by our stockholders. We believe this provision benefits the company by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Provisions in our charter and other provisions of Delaware law could limit the price that investors are willing to pay in the future for shares of our common stock.

Our employment agreements with our executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change of control, which could harm our business, financial condition or results of operations.

Our current executive officers are parties to employment agreements providing for aggregate cash payments of up to approximately $1.3 million at September 30, 2017 for severance and other benefits in the event of a termination of employment in connection with a change of control. The payment of these severance benefits could harm our business, financial condition and results of operations. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with Synlogic.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future; therefore, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We have never declared or paid cash dividends on our common stock. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund our operations. In addition, the terms of any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our

common stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our stock price and trading volume to decline.

Changes in, or interpretations of, accounting rules and regulations could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses and accounting for stock-based compensation, are subject to further review, interpretation and guidance from relevant accounting authorities, including the SEC. Changes to, or interpretations of, accounting methods or policies may require us to reclassify, restate or otherwise change or revise our financial statements, including those contained in this periodic report.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately $ (or approximately $ if the underwriters' 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 fund our two planned Phase 1b / 2a clinical trials of SYNB1020 (one study involving HE patients and the other study involving UCD patients) through completion;
- to fund activities in process development, formulation and toxicology as needed for subsequent initiation of a Phase 2b clinical trial in patients with liver cirrhosis with elevated blood ammonia;
- to fund our planned Phase 1 / 2a clinical trial of SYNB1618 through completion and to support acceleration of a Phase 2b clinical trial of SYNB1618 for PKU patients and continued process development and formulation activities;
- to fund further preclinical development in our immuno-oncology programs and drug discovery activities in our other programs;
- 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 in "Risk Factors." 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.

Based on our current plans, we believe that our existing cash and cash equivalents, together with the net proceeds from this offering, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through .

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. In particular, we anticipate that those funds, while sufficient to initiate the Phase 2 clinical trials described above, will not be sufficient to enable us to complete such planned Phase 2 clinical trials. 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.

PRICE RANGE OF COMMON STOCK

Our common stock has been publicly traded on the Nasdaq Capital Market under the symbol “SYBX” since August 28, 2017, prior to which it was traded under the symbol “MIRN.” On January 22, 2018, the closing price for our common stock as reported on the Nasdaq Capital Market was $10.63 per share. The following table shows the high and low sales prices per share as reported on the Nasdaq Capital Market for the periods indicated.

Fiscal Quarter Ended	High	Low
March 31, 2016	$46.55	$24.99
June 30, 2016	$34.58	$27.72
September 30, 2016	$31.15	$12.74
December 31, 2016	$13.86	$ 7.84
March 31, 2017	$16.45	$11.41
June 30, 2017	$15.05	$ 9.10
September 30, 2017	$23.00	$10.15
December 31, 2017	$20.12	$ 8.76
March 31, 2018 (through January 22, 2018)	$15.00	$ 9.65

As of January 22, 2018, we had 161 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

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 and cash equivalents and capitalization as of September 30, 2017:

- on an actual basis; and
- on an as adjusted basis, giving effect to the sale of shares of common stock by us in this offering for aggregate net proceeds of $, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of September 30, 2017	
	Actual	As Adjusted
	($ in thousands, except share and per share data)	
Cash and cash equivalents	$ 79,175	$
Short-term marketable securities	$ 17,397	
Long term debt	$ 165	$
Shareholders' equity:		
Common stock, $0.001 par value per share; 250,000,000 authorized; 16,284,885 issued and outstanding, actual; shares issued and outstanding, as adjusted	16	
Additional paid-in-capital	155,508	
Accumulated other comprehensive income	(2)	
Accumulated deficit	(59,957)	
Total shareholders' equity	95,565	
Total capitalization	$ 95,730	

The table above excludes:

- 841,510 shares issuable upon the exercise of options outstanding as of September 30, 2017 at a weighted average exercise price of $14.65 per share;
- 48,863 shares reserved for issuance under the Synlogic, Inc. 2017 Stock Incentive Plan; and
- 450,389 shares reserved for issuance under the Synlogic, Inc. 2015 Equity Incentive Award Plan.

In addition, the amounts in the table above assume no exercise by the underwriters of their option to purchase additional shares.

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 September 30, 2017 was approximately $95.6 million, or approximately $5.87 per share of common stock based upon 16,284,885 shares outstanding as of September 30, 2017. 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.

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 net tangible book value as of September 30, 2017 would have been approximately $ million, or $ per share of common stock. This amount represents an immediate increase in 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 September 30, 2017	$5.87	
Increase per share attributable to new investors	$	
As adjusted net tangible book value per share as of September 30, 2017, 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 16,284,885 shares of common stock outstanding as of September 30, 2017, and excludes:

- 841,510 shares issuable upon the exercise of options outstanding as of September 30, 2017 at a weighted average exercise price of $14.65 per share;
- 48,863 shares reserved for issuance under the Synlogic, Inc. 2017 Stock Incentive Plan; and
- 450,389 shares reserved for issuance under the Synlogic, Inc. 2015 Equity Incentive Award Plan.

In addition, the amounts in the table above assume no exercise by the underwriters of their option to purchase additional shares.

If the underwriters exercise their option to purchase shares of common stock in full at the public offering price, the as adjusted net tangible book value after this offering would be approximately $ per share, representing an increase in net tangible book value of approximately $ per share to existing stockholders and immediate dilution in net tangible book value of approximately $ per share to investors purchasing our common stock in this offering at the public offering price.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on advancing our 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 our proprietary drug discovery and development platform. We apply the principles and tools of synthetic biology to engineer beneficial probiotic bacteria to perform or deliver critical therapeutic functions such as compensating for missing or damaged metabolic pathways in patients. 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 or delivering combinations of therapeutic factors.

Our initial focus is on metabolic diseases with the potential to be corrected following oral delivery of a living medicine to the gut. This includes a group of rare genetic diseases called inborn errors of metabolism ("IEMs"), as well as acquired metabolic diseases caused by organ dysfunction. Our approach to selecting these initial programs is based on the potential of the Synthetic Biotic platform to uniquely address conditions in which there is (1) unmet medical need with (2) well understood biology that is (3) based on an imbalance of a metabolite and (4) where that metabolite is available within or originating from the gut lumen. Additional considerations include the availability of animal models, relevant biomarkers and feasible clinical development paths. Our initial clinical and preclinical programs are focused on certain IEMs that share these characteristics. When delivered orally, Synthetic Biotic medicines are designed to act from the gut to compensate for the dysfunctional metabolic pathway with the intended consequence of reducing the systemic levels of the toxic metabolites. We believe that success in IEMs will enable us to demonstrate the potential of our oral Synthetic Biotic medicines to address metabolic dysfunction while bringing meaningful change to the lives of patients suffering from these debilitating conditions.

Our two lead therapeutic programs are being developed for the treatment of hyperammonemia and phenylketonuria ("PKU"). There are unmet needs to improve current therapies for both indications and opportunities to reduce toxic metabolites that originate from the gut. Both also inform the potential of the Synthetic Biotic platform in unique ways. Our lead Synthetic Biotic program is SYNB1020. SYNB1020 is an oral therapy intended for the treatment of patients with. In patients with these conditions ammonia accumulates in the body and becomes toxic leading to neurocognitive crisis and risk of long-term cognitive or behavioral impairment, coma or death. Hyperammonemic conditions include urea cycle disorders ("UCD") which are IEMs and hepatic encephalopathy ("HE") in patients with liver disease. SYNB1020 has received both Fast Track Designation and orphan drug designation for UCD from the U.S. Food and Drug Administration (the "FDA"). We initiated a Phase 1 clinical trial in June 2017 to evaluate the safety and tolerability of SYNB1020 in healthy volunteers. In November 2017, we announced top-line data from this study that demonstrated that SYNB1020 was safe and well-tolerated and achieved proof-of-mechanism. In 2018, we intend to initiate two Phase 1b / 2a studies for SYNB1020 in patients with elevated blood ammonia.

Our second program, SYNB1618, is an oral therapy intended for the treatment of PKU, an IEM in which the amino acid 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. SYNB1618 is designed to have activity in the gut of patients to reduce excess circulating Phe, resulting in normalization of levels in the blood and tissues. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. We are planning to file an investigational new drug ("IND") application and initiate a Phase 1 / 2a clinical trial for SYNB1618 in the first half of 2018.

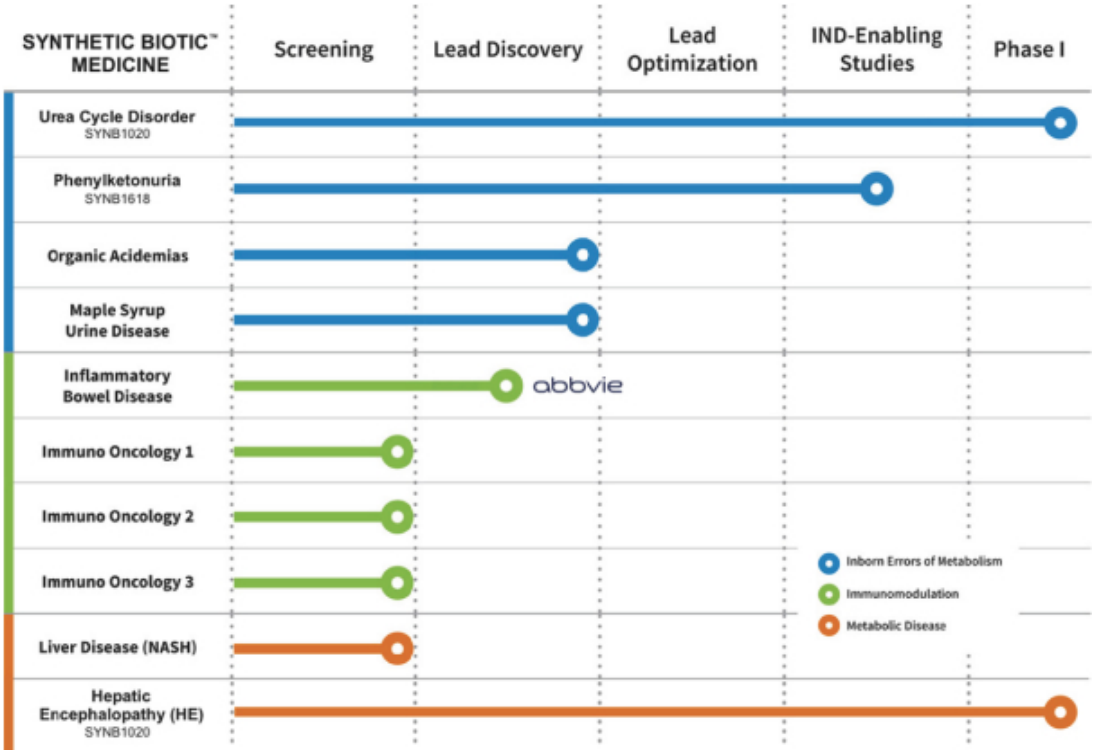
Our early-stage metabolic pipeline includes discovery-stage product candidates for additional IEMs, including maple syrup urine disease ("MSUD"), isovaleric acidemia ("IVA") and organic acidemias. These are rare metabolic deficiencies in which the toxic accumulation of metabolites such as branched chain amino acids in

the case of MSUD can lead to neurological decline and death. There are no currently approved pharmaceutical therapies for these disorders, ultimately resulting in patients relying on liver transplants when possible. We are also leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including acquired metabolic diseases, inflammation and cancer. Synthetic Biotic medicines are designed to locally deliver combinations of complementary therapeutics to treat these complex disease states. Our portfolio of immuno-oncology programs is designed to deliver a combination of activities to modify the tumor microenvironment, activate the immune system and result in tumor reduction. We have established a collaboration with Ginkgo Bioworks, a privately held synthetic biology company, to discover new living medicines to treat neurological and liver disorders. We also have a collaboration with AbbVie S.à.r.l. ("AbbVie") to develop Synthetic Biotic medicines for the treatment of inflammatory bowel disease ("IBD") such as Crohn's disease and ulcerative colitis. While we intend to develop and commercialize therapeutic candidates for the treatment of IEMs on our own, we may consider entering additional strategic partnerships in the future to maximize the value of our programs and our Synthetic Biotic platform.

To progress our pipeline, we collaborate with key disease experts who have developed robust models of relevant diseases to guide selection of our development candidates and to inform our translational medicine strategy. We focus on indications with clear biomarkers associated with disease progression that enable straightforward, early and ongoing assessment of potential clinical benefit throughout the development process. Our collaboration and intellectual property strategies additionally focus on building or leveraging existing third-party expertise in therapeutic research, preclinical and clinical development, regulatory affairs, manufacturing and commercialization, while also enhancing our industry-leading position in synthetic biology and metabolic engineering.

We have assembled a management team of seasoned biopharmaceutical executives with extensive, relevant experience at leading pharmaceutical companies such as Pfizer Inc., GlaxoSmithKline, Biogen, Inc., AstraZeneca, Millennium Pharmaceuticals, Inc. (now Takeda Pharmaceutical Company Limited) and MedImmune, as well as the National Institutes of Health. We are supported by our Board of Directors and our scientific advisory board, each of which offer 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 labs 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.

Our pipeline of programs is shown below.



As we advance our lead programs, we continue to learn and improve the flexibility, manufacturability and translatability of our Synthetic Biotic platform, which will inform all future portfolio programs. Consequently, we believe we have a robust engine for building a sustainable pipeline of novel, living medicines across a range of diseases. Through the strength of our internal team and network of partners, we believe we can deliver on the promise of Synthetic Biotic medicines to improve the lives of patients with significant unmet medical needs.

Our Strategy

Our goal is to use our Synthetic Biotic platform to design, develop and commercialize living medicines to transform the lives of patients for whom conventional treatment approaches are either not available or have limited efficacy and safety. To achieve our goal, we are pursuing the following key strategies:

Rapidly Advance Clinical Development of the SYNB1020 Hyperammonemia Program. Our lead Synthetic Biotic program is for the treatment of hyperammonemic conditions such as UCD and HE. SYNB1020 is an oral therapy designed to deliver a complementary metabolic pathway in the gut with the intended consequence of removing excess ammonia in the blood. SYNB1020 has received orphan drug designation and in June 2017 was granted Fast-Track designation for UCD from the FDA. We initiated our first Phase 1 clinical trial to assess safety, tolerability and pharmacokinetics in healthy volunteers in June 2017. In November 2017, we announced top-line data from this study that demonstrated that SYNB1020 was safe and well-tolerated and achieved proof-of-mechanism. In 2018, we intend to initiate two Phase 1b / 2a studies for SYNB1020 in patients with elevated blood ammonia. We expect to initiate the first study in patients with cirrhosis as a result of liver disease in the first quarter of 2018 and to have data from this study by the end of 2018. In addition, we expect to begin a clinical trial in UCD by mid-2018 with data expected in mid-2019.

Advance SYNB1618 into Clinical Development. Our second IEM program is an oral therapy for PKU. SYNB1618 is designed to act from the gut to convert excess Phe to non-toxic metabolites and thereby prevent Phe from accumulating in the blood, becoming toxic and leading to neurological dysfunction. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. We are planning to initiate a Phase 1 / 2a clinical trial for SYNB1618 in the first half of 2018. The Phase 1 / 2a design will include healthy volunteers, as well as an adult patient cohort, to assess safety, tolerability and pharmacodynamics. We expect to have data from healthy volunteers, including insights from a mechanistic biomarker, by the end of 2018 and insights regarding therapeutic potential by the first half of 2019.

Expand Our Pipeline by Targeting Additional Rare Genetic Metabolic Diseases. We plan to continue to leverage our expertise from our lead programs to accelerate development of our pipeline of clinical candidates for IEMs. For example, our portfolio includes two additional discovery-stage Synthetic Biotic programs in lead optimization, including one for MSUD/IVA and the other for propionic acidemia ("PA")/methylmalonic acidemia ("MMA"), organic acidemias with high unmet need for which there are biomarkers that we believe can guide efficient product development programs.

Maximize the Value of the Synthetic Biotic Platform in Broader Metabolic and Inflammatory Diseases and in Immuno-Oncology Leveraging Strategic Partnerships. Our Synthetic Biotic platform and product discovery and development capabilities offer the potential to generate multiple clinically meaningful treatments for a broad set of metabolic and inflammatory diseases as well as cancer. For these indications, there is opportunity to reset a metabolic or immune dysfunction with a lower risk of systemic toxicity than other modalities. To achieve this, oral Synthetic Biotic medicines can be designed to deliver a combination of mechanisms following oral administration for activity in the gut or intra-tumoral injection and we are establishing a discovery-stage immuno-oncology portfolio.

We expect to continue to explore strategic partnerships that would leverage the complementary capabilities of our partners to develop Synthetic Biotic medicines for these broader groups of patients in need. Our current partnership with AbbVie is focused on the discovery and development of Synthetic Biotic-based therapies for the treatment of IBD, and in June 2017 we announced our first milestone for this program. While we intend to develop and commercialize our programs for IEMs, we may consider entering into additional strategic partnerships to maximize the value of our Synthetic Biotic platform in these more common indications.

Expand the Synthetic Biotic Platform to Lead in the Discovery and Development of Additional Living Medicines and Enabling Technologies. We intend to advance in the field of living medicines by continuing to innovate and broaden the potential of our Synthetic Biotic platform to deliver clinically meaningful benefits for patients. We plan to build on our expertise in design, optimization and manufacturing to further develop the Synthetic Biotic platform as a reproducible and scalable engine for generating a pipeline of product candidates that address a broad range of diseases. We have also established a collaboration with Ginkgo Bioworks, a privately held synthetic biology company, to discover new living medicines to treat neurological and liver disorders.

Protect and Leverage Our Intellectual Property Portfolio and Patents. We believe that we have a broad intellectual property portfolio that includes patents and patent applications relevant to the engineering, development, manufacturing and formulation of human therapeutic products based on synthetic biology and the metabolic engineering of probiotics. We intend to continue to protect and leverage our intellectual property assets by maintenance and expansion of our worldwide portfolio of intellectual property, including through the pursuit of composition of matter and other intellectual property directed to our Synthetic Biotic programs and our technology platform.

Our Focus: Living Medicines

We are developing and advancing a novel approach to creating living medicines—therapeutics designed to sense a local disease context within a patient's body and to respond by metabolizing toxic substances or delivering combinations of therapeutic factors.

We believe living medicines have unique advantages as potential therapeutics. Living biologic cells can carry out functions that cannot be performed by many conventional drug treatments, such as small molecules or antibodies. While many conventional treatments can address one molecular dysfunction, living medicines can compensate for the dysfunction of entire processes or pathways missing in disease and required for health. By contrast to conventional therapeutics that engage a single target, living medicines can be designed to dynamically sense diseased environments and respond with a programmed and combinatorial effect. Moreover, a living medicine can also function "catalytically," as a single living cell can carry out multiple cycles of the intended therapeutic activity during its time in the patient.

Leveraging Synthetic Biology and Metabolic Engineering of Probiotic Bacteria to Produce Living Medicines

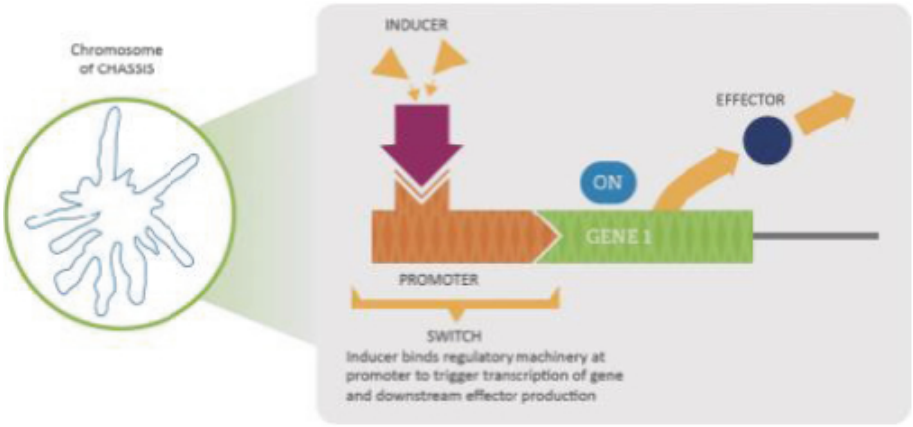
Our proprietary Synthetic Biotic discovery and development platform combines synthetic biology and metabolic engineering to re-design the genetic circuitry of beneficial probiotic bacteria and generate living medicines.

Synthetic Biology

Our proprietary Synthetic Biotic discovery and development platform combines synthetic biology and metabolic engineering to re-design the genetic circuitry of beneficial probiotic bacteria converting them into efficient therapeutic engines and generating living medicines. Probiotic bacteria are non-pathogenic bacteria isolated from the human microbiota widely used as supplements believed to provide health benefits. To confer a therapeutic effect, we leverage basic biological properties of bacteria to develop engineered probiotics. Bacteria have evolved over several billion years to adapt, survive, and carry out active metabolism in many different environments. They are also amenable to genetic manipulation. Our intention is to lead in the discovery and development of Synthetic Biotic therapies as safe living medicines capable of robust and precise pathway complementation and therapeutic benefit.

Our scientists genetically engineer a beneficial probiotic bacterium with "wiring" or biological circuits to direct cellular biological processes in a manner analogous to designing electrical circuits. The critical parts of an engineered Synthetic Biotic medicine include (1) the chassis, or probiotic bacterium, (2) the effector module, which is a gene or pathway encoding the core biological activity that provides the therapeutic function, and (3) tunable switches to precisely determine the circumstances under which the effector module will be activated, as well as the strength, performance and output of the effectors themselves. We aim to precisely control the amount, location and activity of our Synthetic Biotic medicines to address a broad range of disease.

Schematic of the Synthetic Biotic Platform Components: Chassis, Effector, Switch



Metabolic Engineering of Probiotic Bacteria

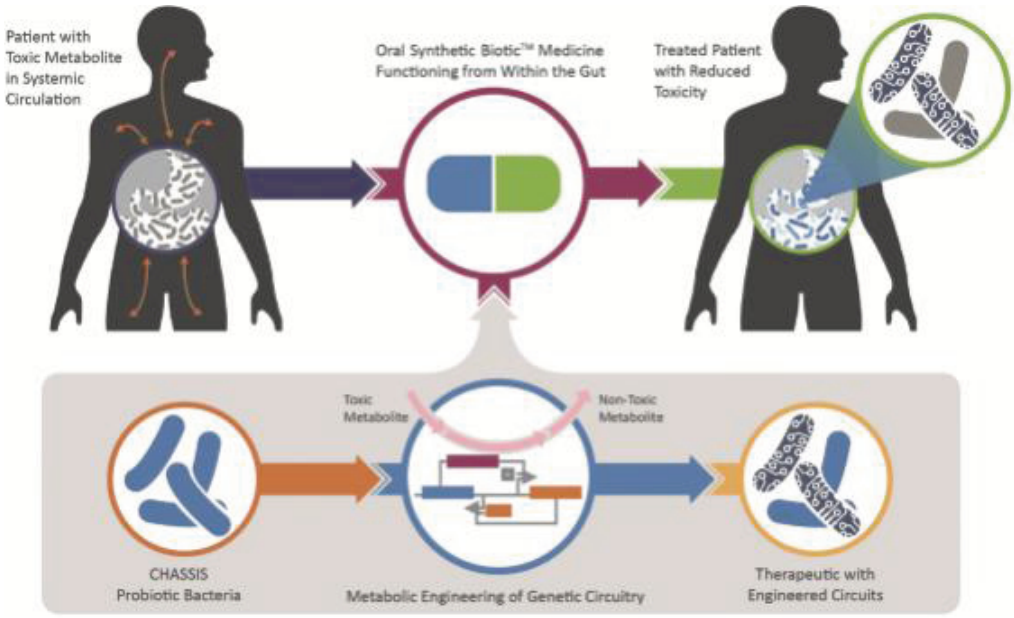
(1) The Chassis: Our Synthetic Biotic platform employs well-characterized bacteria used as probiotics to serve as the chassis upon which we build our living medicines. Our initial programs use *E. coli* Nissle, which is one of many non-pathogenic strains isolated from the human microbiota. *E. coli* Nissle has been used as a probiotic bacterial supplement for the last 20 years to promote gut health. *E. coli* Nissle is a non-colonizing probiotic and has recently been shown in the clinic to be rapidly cleared from most individuals with no significant safety issues (Clin Transl Sci (2017) 00, 1—8). We also observed similar rates of clearance from subjects in our recent Phase 1 clinical trial of SYNB1020 in healthy volunteers. We believe *E. coli* Nissle's widespread use as a probiotic is evidence of its utility as a safe background chassis to apply synthetic biology to confer a therapeutic effect.

(2) Building the Effector Module: E. coli Nissle's metabolic systems are well-understood and extremely adaptable, making it an excellent organism for introducing new or enhanced activities to treat human disease. The highly flexible nature of its genetic and metabolic machinery provides a robust cellular context into which genetic information encoding proteins and pathways to correct for disease can be introduced with high efficiency and little or no damage to the fitness of the bacterium. This provides the potential for excellent reproducibility, stability, and activity during manufacturing. Moreover, the advanced nature of the synthetic biology toolkit available for *E. coli* Nissle enables the rapid iterative design, assembly, and testing of prototype product candidates and remains unique among other bacterial and cellular engineering approaches. We have leveraged proprietary tools, know-how and intellectual property to build multiple Synthetic Biotic lead strains that produce a therapeutically relevant effect in laboratory experiments. Progression of these strains as product candidates in diseases with high unmet need is based on prioritizing those with feasible drug development paths in terms of availability of informative animal models and existence of biomarkers to guide efficient clinical development.

(3) Tunable Switches: We also design and engineer proprietary switches to mediate the activity of the new pathways we introduce, with the aim of controlling the therapeutic output, or effector, of Synthetic Biotic medicines. To optimize the fitness of a Synthetic Biotic strain, it is critical that the effector is activated only at the proper time and place. The switches we have developed are based on engineering DNA elements call "inducible promoters" to sense and respond to disease states, specific environmental signals, or exogenously added inducing molecules. The goal is to discover and develop Synthetic Biotic medicines programmed with switches to produce its therapeutic effect at precisely the right time and location such as the anaerobic environment of the gut, in the context of local inflammation, and in response to other pathogenic factors.

While applicable across metabolic, inflammatory and immuno-oncology indications, our initial Synthetic Biotic programs are designed for rare metabolic diseases in which a metabolite accumulates in the body and causes systemic toxicity. We believe that the Synthetic Biotic platform can be leveraged to engineer a safe probiotic with enhanced genetic circuitry and the capability to transform a toxic metabolite into one that is non-toxic or even beneficial. The resulting Synthetic Biotic medicines are built to be taken orally and function from within the gut. Metabolites produced by both a person's organs and by our endogenous flora circulate or flux between the human gastrointestinal ("GI") tract and blood circulation and vice versa. As our Synthetic Biotic medicines transit through the GI tract, they are designed to have activity in the gut and to take advantage of this flux, ultimately reducing the systemic levels of toxic metabolites in the blood to treat rare metabolic diseases.

Schematic of the Synthetic Biotic Platform to Engineer Probiotic Bacteria



Advantages of Our Synthetic Biotic Living Medicines

We believe our platform has the potential to provide safe and effective therapies for patients given several attributes of our Synthetic Biotic approach:

Unique Mechanisms to Treat Systemic Metabolic and Immune Dysfunction: Local Pathway Complementation or Therapeutic Delivery

Our Synthetic Biotic platform allows us to engineer living medicines that act as engines capable of metabolic pathway compensation and essentially replace what a patient cannot do with his or her somatic organs, such as the liver. Unlike traditional small molecule and biologic therapeutics, Synthetic Biotic medicines can be designed with multiple pathway components optimized to consume or transform unwanted metabolites or produce those that are medically beneficial. This approach is well suited to regulate the amount of a metabolic byproduct in a patient's body, particularly when there is unconstrained metabolite flux between the systemic circulation. Our Synthetic Biotic programs for rare metabolic diseases are designed to be dosed orally, to act locally while transiting through the gut and, as a consequence, to decrease toxic metabolite levels in the blood, thereby providing a systemic therapeutic benefit to the patient.

In addition, we are developing Synthetic Biotic medicines with the potential to normalize function of a dysregulated immune system. In inflammatory and autoimmune indications, this may be achieved by producing anti-inflammatory metabolites and proteins particularly for diseases of the GI tract. Synthetic Biotic medicines can also be designed to consume or produce metabolites or secrete and display proteins that may shift the tumor microenvironment of the immune system towards anti-tumor activity.

Combination and Local Delivery of Multiple Mechanisms in One Therapy for Potential Greater Efficacy and Enhanced Safety

Currently, many complex diseases, such as inflammatory and autoimmune indications and oncology, require that patients be treated with a combination of therapeutic agents, often resulting in poor tolerability, multiple adverse events and increased cost of therapy. Our approach is to leverage the adaptability of *E. coli* Nissle to enable the combination of multiple activities into one therapy, which therefore could have greater efficacy while avoiding the impact of multiple separate systemic therapies.

Moreover, our Synthetic Biotic medicines are based on beneficial probiotic bacteria derived from the natural human gut. A chassis such as *E. coli* Nissle is suited for local delivery, either orally or through intra-tumoral injection. We believe that, when delivered locally, Synthetic Biotic medicines have the potential to avoid the risks of dose-limiting side effects often associated with systemic therapies, especially when combinations of systemic therapies are required.

Ability to Tune and Enhance Efficacy in Context of Disease

Our Synthetic Biotic platform includes a suite of switches to permit precise control of the timing and amount of therapeutic effect produced. Synthetic Biotic therapies may be designed such that they are activated to produce the desired effect in a particular disease environment, such as sites of inflammation. This tuning has the potential to increase the therapeutic window by increasing the margin between the level of medicine needed for efficacy relative to the risk of systemic toxic side effects.

Advantages of Our Synthetic Biotic Drug Development Platform

The Synthetic Biotic platform employs a well-characterized probiotic bacterium with a proven safety record that is readily modified using state-of-the-art synthetic biology tools. This unique combination of features allows us to rapidly develop prototypes for the treatment of human diseases with unmet medical need. Advantages to discovery, development, manufacturing and commercialization, include unique mechanisms of action enabling a broad range of therapeutic applications and rational design to achieve predictable drug-like properties:

Unique Mechanisms of Action Enabling a Broad Range of Therapeutic Applications

Our approach allows us to engineer two types of mechanistic activities into our Synthetic Biotic medicines. These activities may be further improved for therapeutic effect when combined or when under the control of tunable switches that determine when the mechanisms should be activated.

- *Metabolic Pathway Complementation*: Synthetic Biotic medicines may be programmed with entire pathways to degrade unwanted molecules or produce those that are beneficial. We believe metabolic pathway complementation is advantageous as compared to gene, RNA or enzyme replacement therapies that are limited to targeting a single gene or protein defect and may require several unique drug products to address genetically heterogeneous patient populations. By compensating with an entire pathway, Synthetic Biotic medicines may provide a therapeutic solution to broader disease populations as a single engineered therapeutic. Moreover, in the IEM space we believe our approach has advantages versus these other modalities that may be limited by delivery, transduction efficiency, duration of therapeutic expression and unclear potential for long-term dosing. Given the potential for chronic oral dosing, Synthetic Biotic medicines may have benefits in terms of prediction of dose, reversibility of activity and more traditional pricing strategies.

- *Production of One or More Protein Effectors at the Site of Disease*: Combinations of cytokine, antibody and protein therapies have potential for great effect, but can be restricted by dose-limiting side effects when administered systemically. The potential to program the control of expression of one or more proteins at the local disease site represents a unique approach to targeted therapy. We have developed proprietary integration systems to direct stable insertion of multiple genetic circuits and pathways into optimal chromosomal locations, or "landing pads," of *E.* coli Nissle. This enables efficient expression of multiple genes encoding desired enzymes and other proteins. We have also developed approaches to enhance the secretion of protein effectors to the extracellular environment. For example, in the case of inflammatory conditions, Synthetic Biotic medicines may be programmed to detect inflammation and respond with the production of one or more anti-inflammatory molecules. In oncology, our programs are being designed to secrete effectors to promote immune system activity against a tumor. These activities may further be combined with metabolic complementation pathways. By incorporating multiple actions, Synthetic Biotic medicines have the potential to address complex diseases while avoiding the risk of systemic toxicity and reducing development costs associated with combining systemic therapies.

Rational Design to Achieve Predictable Drug-like Properties

We have demonstrated the ability to move a program from concept to clinical development in as little as three years for our lead program. Features of our Synthetic Biotic platform enable a highly efficient drug discovery and development process and have the potential to advance product candidates more rapidly and efficiently than is typically possible with other novel or emerging modalities. These include:

- *Single Strain as Safe Chassis.* There are several benefits of employing a single, safe and well-characterized probiotic bacterium such as *E. coli* Nissle as the background chassis. First, because our lead programs are based on *E. coli* Nissle, experience can be leveraged broadly across the portfolio, further optimizing the efficiency and reproducibility of discovery, development and manufacturing efforts. Next, the non-colonizing nature of *E. coli* Nissle can be combined with engineering approaches to optimize safety in terms of impact on the patient and the environment. *E. coli* Nissle can be engineered to require a specific exogenous nutrient supplement for growth, which limits the ability to replicate in the human body and environment. By controlling replication, we can control the number of cells being administered to a patient. Also, dependence on an essential nutritional supplement not available in the environment reduces biocontainment risk. Moreover, the risk of a Synthetic Biotic medicine to the environment is further limited given that it is disadvantaged in terms of fitness due to its modifications.

- *Predictive Pharmacology and Biomarkers*. Synthetic Biotic programs are designed to achieve a target activity, and the platform supports an iterative design-build-test cycle to improve performance for achieving this target. For example, Synthetic Biotic programs can be optimized by including multiple copies or regulated control of certain genes, by adding transporters for particular substrates or by optimizing enzymes for basic bacterial metabolism. These tools enable rational and iterative engineering cycles in the discovery phase.

  Biomarkers as indicators of mechanistic and clinical activity may also be engineered into Synthetic Biotic medicines from the beginning to drive optimization and decision-making. By assessing the activities of our Synthetic Biotic programs in *in vitro* and *in vivo* preclinical models, we can model activity in humans. As we progress into clinical studies, we expect our predictive pharmacology models will be further refined to inform dosing and development decisions for our additional programs.

- *Stability and Manufacturing*. Our lead Synthetic Biotic programs have advanced the platform by defining manufacturing processes that can be deployed against the entire portfolio. Our use of synthetic biology switches permits the precise control of engineered metabolic pathway activation. We use switches to suppress effector activity during manufacturing, enabling development of reproducible processes for generation of biomass and robust, cost-efficient scale up of product candidates.

Manufacturing efforts have demonstrated reproducibility, yield and stability during small, medium and Phase 1 clinical-scale campaigns and we have developed and executed processes to manufacture 3,000—5,000 doses of active drug.

Our Product Pipeline

Our approach to selecting our initial programs is based on the potential of the Synthetic Biotic platform to uniquely address conditions in which there is (1) unmet medical need with (2) well understood biology that is (3) based on an imbalance of a metabolite and (4) where that metabolite is available within or originates from the gut lumen. Additional considerations include the availability of animal models, relevant biomarkers and feasible clinical development paths. Our initial clinical and preclinical programs are focused on certain IEMs that share these characteristics. When delivered orally, Synthetic Biotic medicines are designed to act from the gut to compensate for the dysfunctional metabolic pathway with the intended consequence of reducing systemic levels of the toxic metabolites. We believe success in IEMs will enable us to demonstrate the potential of our oral Synthetic Biotic medicines to address metabolic dysfunction, while bringing meaningful change to lives of patients suffering from these debilitating conditions.

Our two lead therapeutic programs are being developed for the treatment of UCD and PKU, both IEMs. There are unmet needs to improve current therapies for both indications and opportunities to reduce toxic metabolites that originate from the gut. Both also inform the potential of the Synthetic Biotic platform in unique ways. Our lead Synthetic Biotic program is SYNB1020. SYNB1020 is an oral therapy intended for the treatment of patients with hyperammonemia. In patients with these conditions ammonia accumulates in the body and becomes toxic leading to neurocognitive crisis and risk of long-term cognitive or behavioral impairment, coma or death. Hyperammonemic conditions include UCD which are IEMs and HE in patients with liver disease. SYNB1020 has received both Fast-Track designation and orphan drug designation for UCD from the FDA. We initiated a Phase 1 clinical trial in June 2017 to evaluate the safety and tolerability of SYNB1020 in healthy volunteers. In November 2017, we announced top-line data from this study that demonstrated that SYNB1020 was safe and well-tolerated and achieved proof-of-mechanism. In 2018, we intend to initiate two Phase 1b / 2a studies for SYNB1020 in patients with elevated blood ammonia. Our second program, SYNB1618, is an oral therapy intended for the treatment of PKU, an IEM in which 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. SYNB1618 is designed to have activity in the gut of patients to reduce excess circulating Phe, resulting in normalization of levels in the blood and tissues. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. We are planning to initiate a Phase 1 / 2a clinical trial for SYNB1618 in the first half of 2018.

Our early-stage metabolic pipeline includes discovery-stage product candidates for additional IEMs, including MSUD, IVA and organic acidemias. These are rare metabolic deficiencies in which the toxic accumulation of metabolites such as branched chain amino acids in the case of MSUD can lead to neurological decline and death. There are no currently approved pharmaceutical therapies for these disorders, ultimately resulting in patients relying on liver transplants when possible. We believe that developing therapies for this group of rare diseases will demonstrate the potential of our oral Synthetic Biotic medicines to address metabolic dysfunction, while bringing meaningful change to lives of patients suffering from these debilitating conditions. We are also leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including acquired metabolic diseases, inflammation and cancer. We are developing a portfolio of immuno-oncology programs using a rational approach to select combinations of relevant mechanisms to address specific tumor types. Our strategy is to alter the state of the tumor microenvironment to one that is “anti-tumor” through Synthetic Biotic medicines that consume or combine effectors that promote immune system activation, reverse immunosuppression, expand tumor antigen-specific T cells and/or remodel the tumor protective stroma to tip the balance toward an anti-tumor effect. We are currently working on three discovery-stage programs, which are diversified in terms of indications, combinations of mechanisms and routes of administration. We also have a collaboration with AbbVie to develop Synthetic Biotic medicines for the treatment of IBD. We have also established a collaboration with Ginkgo Bioworks to discover new living medicines to treat neurological and liver disorders.

Our Initial Programs: Overview of IEMs

Patients with IEMs are born with faulty genes that result in the loss of a necessary enzyme function in an essential metabolic pathway and prevent the body from metabolizing commonly occurring byproducts of digestion. In patients with IEMs, these byproducts can accumulate to toxic levels in the gut and systemically throughout the body to cause serious health consequences, including irreversible neurological dysfunction. Although in some cases diet modification can be beneficial, unmet medical need remains as there are few current treatments for IEMs.

While there are hundreds of genetic conditions grouped as IEMs, individual IEMs are considered orphan diseases, with each disease affecting fewer than 200,000 patients in the United States and fewer than five per 10,000 people in the European Union. IEMs include diseases of the urea cycle, amino acid metabolism and organic acid accumulation, among others. Many IEMs are thought to be underdiagnosed given the rarity of the conditions, potential for infant death, lack of available diagnostics and limited therapies.

SYNB1020 for Hyperammonemia: Urea Cycle Disorders and Hepatic Encephalopathy

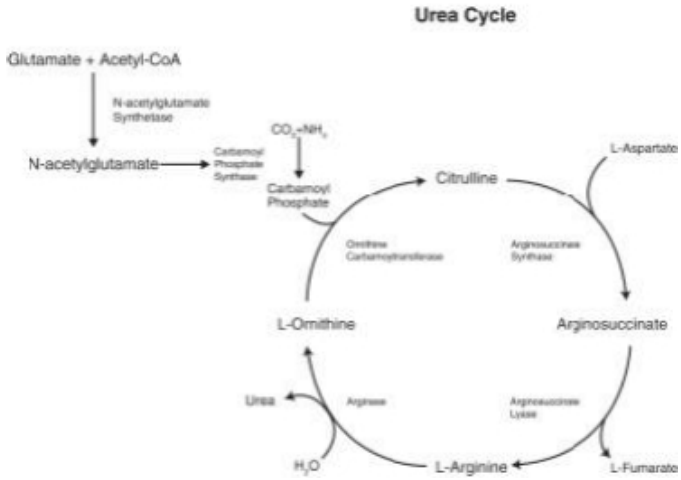
Hyperammonemia is a metabolic condition characterized by an excess of ammonia in the blood. In healthy individuals, ammonia is primarily produced in the intestine as a byproduct of protein metabolism and microbial degradation of nitrogenous-containing compounds. Ammonia itself is then converted to urea in the liver and is excreted in urine. However, if the liver's ability to convert ammonia to urea is compromised, either due to a genetic defect or acquired liver disease, ammonia accumulates in the blood. Elevated blood ammonia levels are toxic to the brain and can have severe consequences including neurologic crises requiring hospitalization, irreversible cognitive damage and death.

SYNB1020, our lead Synthetic Biotic program, is a genetically engineered strain of *E. coli* Nissle designed to deliver a complementary metabolic pathway to the gut to reduce excess ammonia in the blood in individuals with disease. The SYNB1020 program offers potential in treating multiple indications associated with toxic ammonia levels, including UCD and HE, and has demonstrated reduction in blood ammonia levels in rodent models of hyperammonemia. SYNB1020 has received orphan drug designation and in June 2017 was granted Fast-Track designation for UCD from the FDA. The FDA Office of Vaccines Research and Review (CBER) has advised us that the clinical development of SYNB1020 does not require submission to the NIH RAC, a committee that reviews human gene transfer protocols and that lowering of blood ammonia level is an approvable end-point for UCD. We initiated a Phase 1 clinical trial of SYNB1020 in healthy volunteers in June 2017. In November 2017, we announced top-line data from this study that demonstrated that SYNB1020 was safe and well-tolerated and achieved proof-of-mechanism. In 2018, we intend to initiate two Phase 1b / 2a studies for SYNB1020 in patients with elevated blood ammonia.

Overview of UCD

UCDs are a group of rare but serious and potentially fatal, genetic diseases. The urea cycle is an enzymatic pathway in which waste nitrogen, produced as a byproduct of protein metabolism, is converted into urea by the liver and eliminated from the body through urine. Patients with a UCD carry a deficiency in one of the six enzymes necessary for completion of the urea cycle, resulting in accumulation of waste nitrogen throughout the body in the form of ammonia, a substance that is highly toxic even in small amounts.

Functional Urea Cycle



UCD patients have intermittent periods of hyperammonemia, the symptoms of which can range from mild (loss of appetite, vomiting, and lethargy) to a severe hyperammonemic crisis associated with long-term cognitive or behavioral impairment, toxic encephalopathy, and even death. Symptoms often depend on the severity of the enzyme deficiency, and patients with the most severe disease present shortly after birth. Hyperammonemia in newborn infants due to UCD could be catastrophic and is associated with 24% mortality. Patients with later onset disease could suffer from a period of hyperammonemia that is often triggered by stress or illness (surgery, trauma, or drugs) resulting in severe neurological symptoms and associated with a high risk of mortality.

While it is difficult to estimate the exact incidence and prevalence of UCD, as it is thought that many patients go undiagnosed, it is estimated that UCD occurs in approximately one in 35,000 births in the United States. Based on analysis of the newborn screening data and demographic data from the UCD Longitudinal Registry Study sponsored by the NIH, we believe the size of the diagnosed prevalent population in the United States to be approximately 2,000 patients and that approximately two-thirds of these patients are under 18 years of age.

The mainstay of management of UCD is dietary protein restriction. Patients must carefully balance their protein intake to ensure the body receives adequate nutrients for growth and development, while avoiding triggering hyperammonemia. However, varying protein requirements and variable growth and activity levels often elicit episodes of hyperammonemia that can result in irreversible neurological damage. To supplement for the lower protein intake, patients may incorporate amino acid dietary formulations, such as L-citrulline or L-arginine, into their diet. However, dietary management remains challenging, especially in infants and children.

The only available drugs, Buphenyl® (sodium phenylbutyrate) and Ravicti® (glycerol phenylbutyrate), are approved for the chronic management of patients with UCD and create an alternate pathway for nitrogen/ammonia elimination from the body, but patients maintain protein restricted diets. Use of sodium phenylbutyrate is limited by pill burden, taste, and tolerability issues that can make compliance challenging. These therapies are mechanistically similar treatment options with limitations on maximal effect due to dose-related neurological safety issues (e.g., vomiting, nausea, headache, somnolence, confusion, or sleepiness) and enzymatic saturation and, therefore, the unmet need remains high.

When these management approaches fail to control chronic UCD-induced hyperammonemia, patients may be candidates for liver transplantation, which is potentially curative as it may correct the enzyme deficiency that causes UCD. However, aside from being very costly, transplants are limited by availability of donor organs, are

associated with potentially life-threatening risks and require life-long suppression of the immune system. Ultimately, morbidity and mortality remain high in UCD, and patients continue to suffer hyperammonemic crises. We believe that a truly transformative therapy for UCD would be an effective oral medicine without systemic toxicity that will maintain blood ammonia concentration at a safe level while allowing patients to eat a normal or only moderately restricted diet.

Overview of HE

The primary function of the liver is to filter out toxins, particularly ammonia, that are harmful if not sufficiently metabolized. In patients whose liver function is impaired, these toxins can accumulate in the blood stream and cause organ damage, particularly in the brain, which leads to a decline in brain function that is referred to as HE. Ammonia, a highly toxic substance produced in the body as a byproduct of protein metabolism, plays a key role in the development and prognosis of HE. While ammonia can be minimally metabolized by the brain in patients whose liver function is impaired, excessive ammonia levels can overwhelm the capacity of brain tissue and lead to a greater chance of developing brain swelling, coma and death for patients with HE. It is estimated that 30-45% of patients with chronic liver disease are affected by episodes of HE, and while many HE symptoms can be reversed with appropriate treatment, persistent impairment of memory and learning can occur.

HE severity is typically classified as covert or overt based largely on a patient's mental state. Covert HE is difficult to diagnose and is often observed in patients with cirrhosis who appear to have no obvious disorientation, but who display mild to moderate symptoms, such as difficulty concentrating, forgetfulness, changes in personality or behavior, and poor sleep. Patients with covert disease are at a higher risk of developing the more severe overt HE and have increasingly been recognized as a cause of morbidity linked with increased risk of traffic accidents and unemployment. Overt HE is associated with obvious mental disorientation and physical symptoms such as lethargy, seizures, tremors, organ failure, or brain swelling, that arise suddenly and may induce a coma or even death, particularly if not adequately treated. Overt HE is associated with a poor prognosis, with one-year survival estimates of 20% to 55%.

The current standard of care for overt HE includes lactulose, a non-absorbable disaccharide that prevents the absorption of ammonia in the gut. Lactulose is associated with GI side effects including both painful abdominal cramping and diarrhea. Non-absorbable antibiotics are also used to treat HE, often concurrently with lactulose. Xifaxan® (rifaximin), a broad-spectrum antibiotic used to reduce growth of bacteria that produce ammonia in the colon, was approved for HE based on improvements in the duration of remission, reduced hospitalizations over six months, and improved quality of life in patients with HE. Although rifaximin and lactulose are used therapeutically for overt HE, there are no approved treatments for covert HE.

Morbidity and mortality associated with overt HE remains high and hospitalizations for HE impose a high burden on community resources. When current therapies fail to control overt HE, patients may be candidates for a potentially curative liver transplantation. However, aside from being costly, transplants are limited by availability of donor organs and are associated with potentially life-threatening risks and require life-long suppression of the immune system. There is a need for an effective therapy for patients with HE to stave off episodes of cognitive dysfunction and hospitalizations.

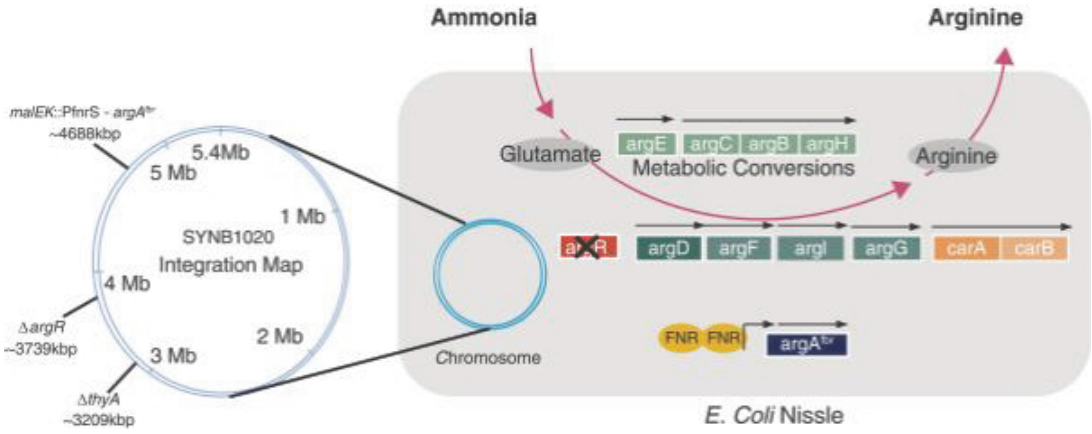
We believe that because ammonia is produced in the GI tract, a Synthetic Biotic medicine could be an effective therapeutic to reduce the levels of excess ammonia in the blood of patients with UCD and HE without the need for severe protein restriction and risk of systemic toxicities.

SYNB1020 Design

SYNB1020, our lead Synthetic Biotic program, is an orally administered, engineered strain of *E. coli* Nissle. SYNB1020 was designed to complement the missing enzyme functions in patients with UCD with an enhanced pathway to consume ammonia, thus having the potential to treat the spectrum of enzyme deficiencies that underlie UCD. This mechanism also has applicability in liver disease where there is a need to reduce excess ammonia in the colon before it can be absorbed into the blood and cause HE episodes.

Our approach was to create a Synthetic Biotic medicine that would continuously consume excess ammonia where it is naturally produced in the colon, before it can be absorbed into the blood, and produce arginine. Arginine production is deficient in UCD patients due to a defect in the urea cycle, and patients are often treated with arginine supplements. *E. coli* Nissle has an endogenous arginine production pathway that uses four molecules of ammonia for every new molecule of arginine produced. We modified this pathway to significantly enhance arginine production function through two key modifications: (1) deletion of a gene that represses the production of the arginine biosynthetic enzymes (*argR*) and (2) insertion of a gene that encodes a feedback-resistant enzyme in the arginine biosynthesis pathway (“ *argA fbr* ”). To enhance activity, *argA fbr* is placed under the control of an inducible promoter, FNR, to allow expression of the gene when the cell experiences micro-aerobic or anaerobic environments, such as the mammalian gut.

Schematic of SYNB1020

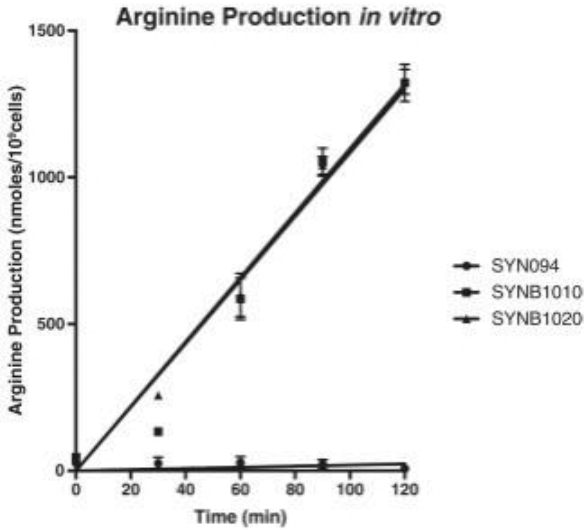


Abbreviations: argA = N-acetylglutamate synthase gene; argA fbr = feedback resistant N-acetylglutamate synthase; ArgB = acetylglutamate kinase; ArgC = N-acetyl glutamylphosphate reductase; ArgD = N-acetylornithine aminotransferase; ArgE = acetylornithine deacetylase; ArgFI = ornithine carbamoyltransferase; ArgG = arginosuccinate synthase; ArgH = arginosuccinate lyase; argR = arginine repressor gene; CarAB = carbamoylphosphate synthetase; FNR = fumarate and nitrate reductase; P fnrS = fumarate and nitrate reductase regulator sensor promoter; D thyA = thymidylate synthase such that the strain can only grow in thymidine-rich environments. Arrows denote operons.

SYNB1020 Nonclinical Program

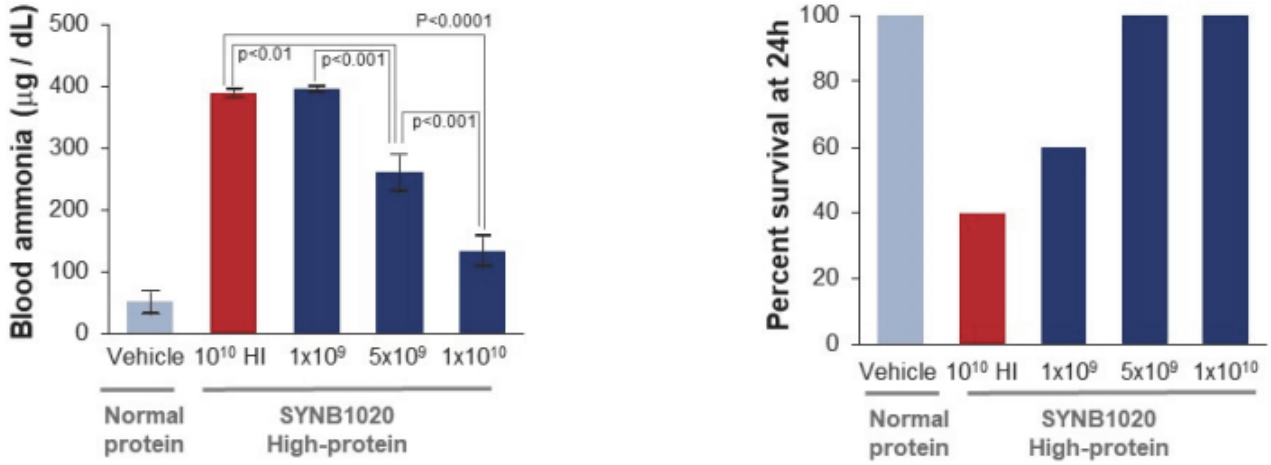
In an *in vitro* study, SYNB1020 and a related research strain SYNB1010 (identical to SYNB1020 except designed to grow in the presence of kanamycin for selection and use in preclinical studies) consumed ammonia and produced arginine at substantially higher rates compared with a control strain of *E. coli* Nissle that had not been engineered (“SYN94”). Arginine production was 650.1 and 658.7 nmol/10 9 cells/hour for SYNB1010 and

SYNB1020, respectively, and only 11.8 nmol/10 9 cells/hour for the control strain. Similarly, conversion of ammonia to arginine was 2545 and 2570 nmol/10 9 cells/hour for SYNB1010 and SYNB1020, respectively, and 46 nmol/10 9 cells/hour for the control strain.



Preclinical Efficacy

To test the *in vivo* activity in a setting of hyperammonemia, the spf-ash/F1 mouse was adapted from a published model based on a mutation in the gene for ornithine transcarbamylase ("OTC"), a common deficiency in human UCDs. A dose-dependent decrease in blood ammonia was observed in mice fed a high protein diet who received orally administered SYNB1020 compared to heat inactivated SYNB1020 at the highest dose. This reduction in blood ammonia resulted in improved survival of animals dosed with SYNB1020, compared to animals given the heat-inactivated control.



SYNB1020 lowers blood ammonia levels in a dose-dependent manner and increases survival in a mouse model of UCD

Preclinical Safety Study

In a GLP 28-day mouse toxicology study, SYNB1020 was safe and well tolerated. No toxicity was detected at the highest feasible dose, and there was no evidence of distribution of SYNB1020 outside the GI tract. Consequently, the no observed effect level was equal to the maximum feasible dose that could be administered, a threshold defined by volume limitations permitted in animals. This represents a greater than 1,000-fold safety margin over the starting dose planned in the Phase 1 study.

SYNB1020 Clinical Development Plan

In June 2017, we initiated a Phase 1 trial to evaluate the safety, tolerability, and gastrointestinal clearance of single and multiple doses of SYNB1020 in healthy volunteers. In November 2017, we announced top-line data that demonstrated that SYNB1020 was safe and well-tolerated in healthy volunteers for up to 14 days and achieved proof-of-mechanism. The Phase 1 trial was a randomized, double-blind, placebo-controlled trial of orally administered SYNB1020 evaluating ascending doses each administered on a single day and multiple ascending doses administered over 14 days. The primary objective of the trial was to assess safety and tolerability of SYNB1020 in healthy volunteers. Secondary objectives were to characterize the microbial kinetics of SYNB1020 in feces as measured by quantitative polymerase chain reaction (“qPCR”) and gastrointestinal tolerability assessed by the Gastrointestinal Symptom Rating Scale. Exploratory endpoints were designed to evaluate the pharmacodynamic effects of SYNB1020, including measurements of blood ammonia levels and other related biomarkers.

Fifty-two healthy volunteers were dosed orally with either SYNB1020 or placebo (ratio three to one), including 28 in seven cohorts in the SAD portion of the study and 24 subjects in three cohorts of the MAD portion of the trial. Complete safety results from the SAD and MAD Phase 1 trials demonstrate that SYNB1020 was well tolerated at total daily doses up to 1.5x1012 CFU for 14 days. Higher doses were associated with mild to moderate gastrointestinal symptoms, mainly nausea and vomiting.

As expected, we did not observe changes in blood ammonia levels during the trial, as all subjects were healthy volunteers who entered the trial with well-controlled normal levels of the metabolite. In a stable-isotope tracer study in which subjects were orally administered 15N-ammonium chloride, we observed a dose-dependent increase in 15Nitrate, a terminal metabolite of arginine, in plasma and urine compared to baseline in SYNB1020-treated subjects but not in the placebo group (see figure below). In subjects treated with the highest dose the increase in blood and urinary nitrate was statistically-significant compared placebo-treated subjects. This observation is consistent with SYNB1020’s mechanism of action which converts ammonia into arginine.

In addition to demonstrating that SYNB1020 was active in vivo, we obtained data on the exposure and clearance of SYNB1020 in treated subjects. We observed that steady-state qPCR copy number increased with increasing SYNB1020 dose and that the bacteria behave in a consistent and predictable way with all subjects clearing within two weeks after the final dose.

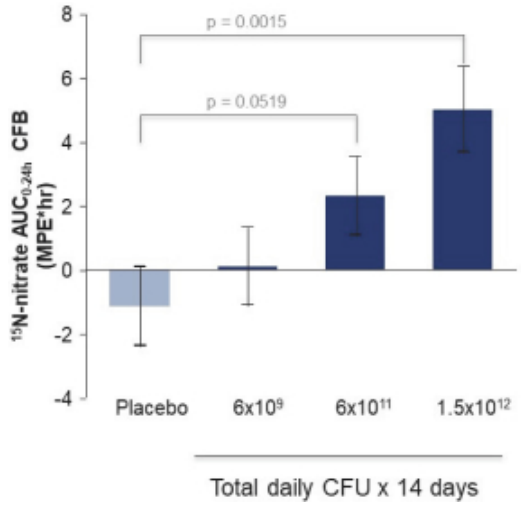
SAD Phase 1 Results

In the SAD trial, a total of 28 healthy volunteers in seven cohorts received total daily doses of SYNB1020 ranging from $2x10^9$ to $6x10^{12}$ CFU, or placebo (ratio three to one). Subjects received a single dose or three doses on a single day. The maximum tolerated total daily dose was 1.5×10^{12} CFU. There were no SAEs reported, with all AEs being mild to moderate, the most common being nausea and vomiting at the highest doses. Three subjects at the highest dose cohorts discontinued dosing.

MAD Phase 1 Results

In the MAD portion of the trial, a total 24 healthy volunteers in three cohorts were dosed three times per day with SYNB1020 at total daily doses of up to 1.5x10^{12} CFU, or with placebo (ratio three to one), for 14 days. No SAEs were reported; higher doses were associated with mild gastrointestinal symptoms, mainly nausea and vomiting during the first week of dosing. One subject in the highest dose cohort discontinued dosing. A dose-dependent increase in nitrate was observed in blood and urine of treated subjects which was found to be statistically significant in the highest dose cohort compared to placebo. The observed dose-dependent changes are consistent with SYNB1020's mechanism of action.

A



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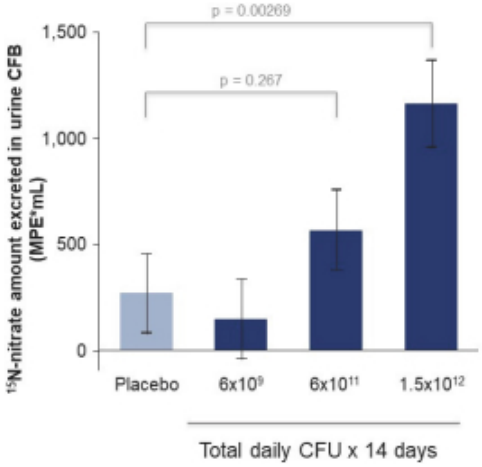


Significant Dose-Dependent Effect on Plasma (A) and Urinary (B) ^{15}Nitrate in SYNB1020 treated healthy volunteers (MPE= molar percent excess)

SYNB1020 Clinical Development Plans and Upcoming Milestones

In 2018, we intend to initiate two Phase 1b / 2a clinical trials to evaluate SYNB1020 in patients with elevated blood ammonia. We expect to initiate the first study, in subjects with liver cirrhosis with elevated blood ammonia, in the first quarter of 2018 and to have data by the end of 2018. The second study in patients with UCDs will begin in mid-2018 and we expect to have data in 2019.

SYNB1618 for PKU

PKU is a rare IEM caused by a genetic defect in the gene phenylalanine hydroxylase ("PAH") leading to Phe accumulation in the blood and brain, where it is neurotoxic and can lead to neurological deficits and even death. Current disease management of PKU involves dietary protein restriction with the consumption of phenylalanine-free protein supplements. The only approved medication, Kuvan ® (sapropterin dihydrochloride) is indicated for a subgroup of patients and does not eliminate the need for ongoing dietary management. Despite recommendations supporting life-long control of phenylalanine levels, compliance is challenging due to the highly restrictive nature of the diet, putting patients at risk for cognitive and psychiatric disease and supporting the need for novel treatment approaches.

Our Synthetic Biotic platform is well-suited to complement the missing enzyme function in PKU patients by providing alternative metabolic pathways to consume Phe. Our second IEM program, SYNB1618 for PKU, is designed to remove excess Phe from the blood by transforming it into non-toxic metabolites. SYNB1618 has

demonstrated activity in a rodent model of PKU. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. We are planning to initiate a Phase 1 / 2a clinical trial for SYNB1618 in the first half of 2018.

Overview of PKU

Phe is an essential amino acid that enters the body primarily through dietary protein, and can be toxic if not sufficiently broken down and eliminated. The metabolism of Phe by the liver is dependent on adequate function of the liver enzyme PAH and the cofactor tetrahydrobiopterin ("BH4") necessary for its activity. When the PAH gene is mutated and/or the production of BH4 is blocked, Phe cannot be sufficiently broken down and accumulates to toxic levels (i.e., hyperphenylalaninemia), which can cause irreversible brain damage. PKU is an inherited metabolic disease that presents as a severe form of hyperphenylalaninemia.

The disease course of PKU typically involves worsening neurological function that begins in infancy or early childhood. The clinical manifestations vary depending on severity of the enzyme mutation, the time of diagnosis and treatment initiation, and compliance. Symptoms may be extensive, such as severe cognitive impairment, or they may reflect more moderate neurocognitive or physical issues, such as below average intelligence, behavioral or mood disorders, memory loss, difficulty concentrating, decreased motor function, eczema, body odor, and tremors or seizures. A woman with PKU who becomes pregnant could develop maternal PKU if her diet is not strictly controlled, and there is a risk that the baby will be born with one or more birth defects such as cognitive impairment, microcephaly or congenital heart disease.

Based on the success of newborn screening efforts that began in developed countries in the 1960s, it is believed that nearly all PKU patients under the age of 40 have been diagnosed at birth. The National PKU Alliance estimates that in the United States there are currently 16,500 people living with PKU.

Currently, management of PKU requires a heavily modified diet that restricts protein intake, in order to minimize consumption, combined with essential amino acid and vitamin supplementation. Special medical foods, including phenylalanine-free protein formula, provide patients with dietary protein and fulfill other nutrient needs. However, it is challenging for most PKU patients to adhere to the restricted diet to the level that provides the necessary control of phenylalanine levels even with the efforts of supportive family and social networks. Patients often have trouble adhering to the diet, with particular challenges arising during times of increasing independence during adolescence. Furthermore, access to low protein foods can be challenging, as they are costlier and less nutritious than their higher protein, non-modified counterparts.

Kuvan® (sapropterin dihydrochloride) was the first drug approved for the treatment of PKU in 2007. It is indicated for the reduction of blood phenylalanine in patients with hyperphenylalaninemia with residual PAH activity as it is a synthetic form of the BH4 cofactor. Oral administration of Kuvan, along with protein restriction, has lowered phenylalanine levels in patients who have residual PAH activity and/or mild forms of the disease, which accounts for approximately 20-50% of the PKU population. However, Kuvan does not eliminate the need for ongoing dietary management in all patients. Large neutral amino acids have also demonstrated activity in blocking absorption of excess phenylalanine by the intestines and brain, but are currently only administered in adolescents and adults.

A pegylated form of recombinant phenylalanine ammonia lyase ("PAL"), called Pegvaliase, an enzyme that metabolizes phenylalanine but does not require cofactor activity, is in clinical development for PKU and is not yet approved. While daily Pegvaliase injections have been proven to lower phenylalanine levels regardless of whether patients are following a low protein diet or not, many patients experience injection site reactions and/or develop antibodies to the enzyme, which limits its effectiveness.

Despite recent improvements in PKU therapy, patients continue to suffer from poor outcomes. Even patients who are diagnosed and treated early have increased risk of neurocognitive abnormalities and psychiatric complications and are burdened by the life-long struggle to comply with strict dietary modifications. Available drug therapies demonstrate limited effectiveness, are accompanied by immunologic and other toxicities, and may still require patients to maintain a heavily restricted diet. We believe a truly transformative therapy would be orally-dosed and provide sustained, safe concentrations of phenylalanine while allowing for a normal or only

moderately restricted diet. We believe that a Synthetic Biotic medicine could be an effective oral therapeutic that acts from the gut to transform excess phenylalanine with the consequent effect of reducing levels in the blood without the need for severe phenylalanine restriction or risk of systemic toxicities.

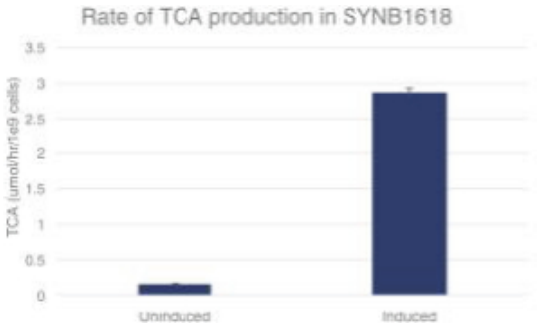
SYNB1618 Design

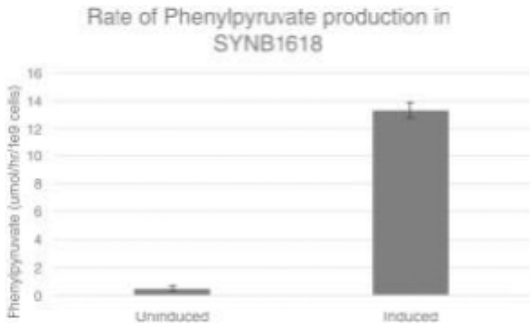
SYNB1618 is a genetically-modified strain of *E. coli* Nissle engineered to express a synthetic pathway for transporting and metabolizing Phe in patients with PKU following oral administration. SYNB1618 was designed to overcome the missing enzyme function in patients with PKU with an alternative pathway to reduce phenylalanine levels.

In designing SNYB1618, we integrated genes encoding the phenylalanine transporter ("PheP"), PAL derived from *Photorhabdus luminescens* and L-amino acid deaminase ("LAAD") derived from the organism *Proteus mirabilis* into the *E. coli* Nissle genome. PheP transports phenylalanine into the Synthetic Biotic bacterial cell with high efficiency, while within the cell PAL converts phenylalanine to the non-toxic byproduct TCA, which is converted in the liver to hippurate and excreted in the urine. The inclusion of multiple copies of these genes further enhanced activity. Similar to PAL, LAAD converts phenylalanine to a non-toxic byproduct, phenylpyruvate, and was designed to provide additional activity in the upper GI.

SYNB1618 Nonclinical Program

We have demonstrated that SYNB1618 can metabolize phenylalanine *in vitro* using both the PAL and LAAD enzymes by measuring their respective non-toxic byproducts. We compared the activity of SYNB1618 under conditions in which the Synthetic Biotic strain is induced (in the "ON" state) versus when uninduced when metabolic activity is suppressed. As shown in the graphs below, *in vitro* activation of PAL led to an 18.5-fold increase in production of the TCA metabolite over uninduced levels, and *in vitro* activation of LAAD led to production of phenylpyruvate levels at 26.7-fold over uninduced levels.



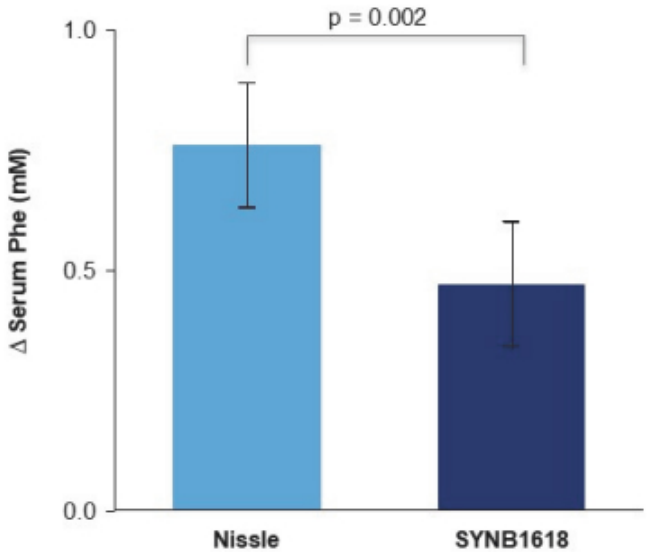


Preclinical Efficacy Studies

In vivo studies have focused on the enu2-/- mouse model that contains a mutation in the gene coding for PAH, the same enzyme that is deficient in PKU patients. Mice with this genetic defect maintained on normal chow accumulate Phe in their blood at concentrations greater than 2000 µM, which is similar to blood concentrations found in humans with PKU. On a Phe-restricted diet, blood Phe levels can be maintained at the healthier range of 100-200 µM.

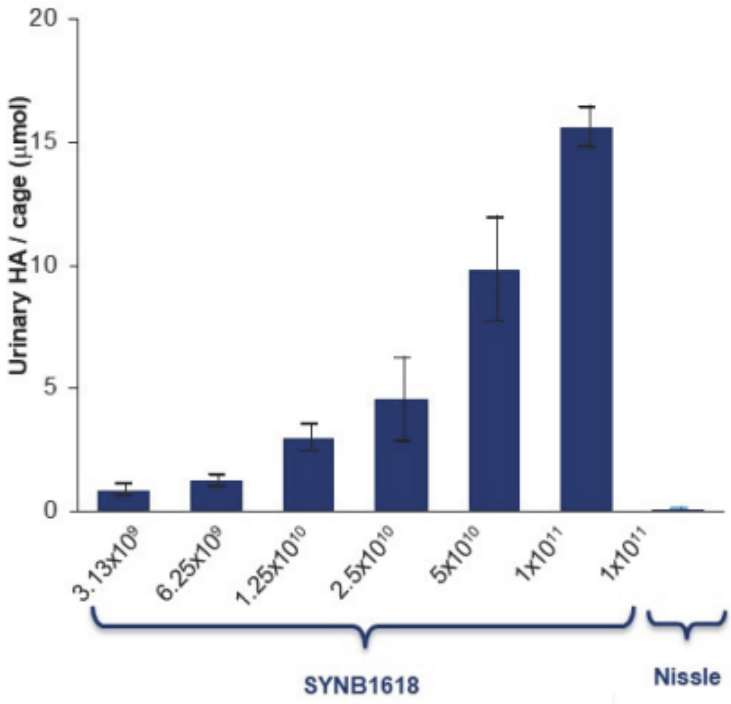
Subcutaneous injection of phenylalanine-restricted mice with phenylalanine results in a rapid increase in blood phenylalanine concentrations. As shown in the graph below, the increase associated with this phenylalanine challenge was significantly blunted upon oral administration of SYNB1618 (5 x 10^{10} CFU) compared to administration of the non-engineered control strain (dose) that did not have the phenylalanine degradation pathway.

Table of Contents



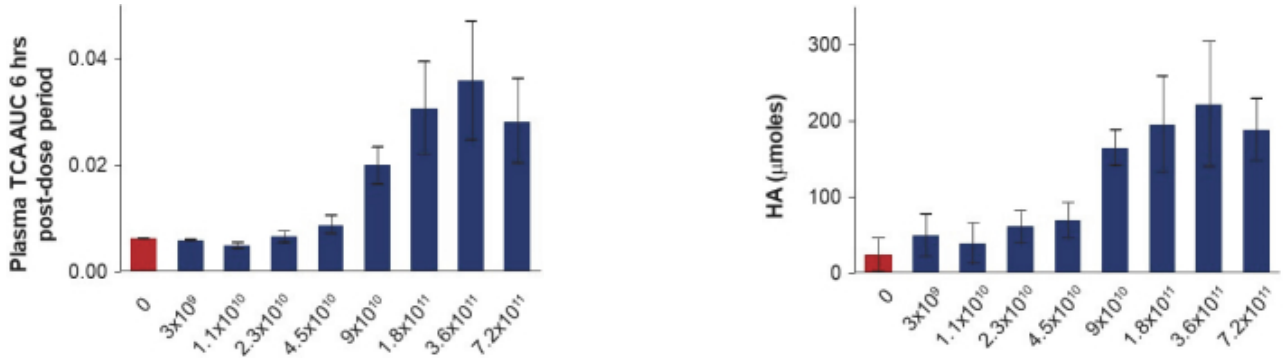
Reduced plasma Phe in Pah^{enu2} mice treated with SYNB1618 (5 x 10^{10} CFU)

One product of Phe degradation by SYNB1618, TCA, is converted to hippurate by liver enzymes and excreted in the urine and can be followed as a urinary biomarker of Phe degradation. Following treatment of *enu2-/-* mice with SYNB1618, urinary hippurate concentration increased in a dose-dependent fashion compared to mice treated with an unengineered *E. coli* Nissle control.



Dose-responsive urinary hippuric acid production in Pah^{enu2} mice

Taken together, these data show that SYNB1618 has activity in the GI tract, and that degradation of recirculating phenylalanine is effective in decreasing the levels found in blood, independent of dietary intake. We have also demonstrated a dose-response in non-human primates with our clinical candidate strain SYNB1618. With increasing oral doses of this single strain, we observe increasing levels of plasma TCA and urinary hippurate.



Preclinical Characterization in Healthy NHPs: Dose-dependent conversion of Phe to plasma TCA and urinary hippurate

These data indicate that SYNB1618 is functional in the environment of the primate gut.

SYNB1618 Clinical Development Plan

In the first half of 2018 we plan to initiate a Phase 1 / 2a, randomized, double-blinded, placebo-controlled study to evaluate the safety, tolerability, and gastrointestinal clearance of SYNB1618. We expect to treat healthy adult volunteers with single- or multiple-ascending doses of SYNB1618 and subsequent cohorts of subjects with PKU.

In addition to the primary endpoint of safety and tolerability, this study will evaluate the change from baseline in several pharmacodynamic parameters compared to placebo in order to characterize the kinetics of SYNB1618 in humans, and provide mechanistic and clinical insights regarding urinary hippurate production and phenylalanine reduction.

Synthetic Biotic Medicines for Additional IEMs

The design, preclinical research, clinical planning and scalable manufacturing of our lead programs have already informed development of future clinical candidates. Our initial programs were selected based on applicability of the Synthetic Biotic platform to provide pathway complementation in IEMs in which the toxic metabolite was known to be associated with the relevant clinical endpoint and to be accessible in the GI tract. Additional examples in which there is opportunity to expand the potential of Synthetic Biotic medicines include discovery-stage programs for (1) MSUD and IVA and (2) PA and MMA. These are rare metabolic deficiencies in which a toxic metabolite can accumulate and lead to neurological decline and death. There is no approved therapy for these diseases and these patients are managed with dietary modifications, supportive care, and liver transplant when available.

A Synthetic Biotic Program for Maple Syrup Urine Disease and Isovaleric Acidemia

MSUD is an IEM that was first described in the 1950s as an inherited progressive neurological degenerative disorder. Patients with this disease have mutations in one of the protein subunits of the mitochondrial

multi-enzyme complex called branched-chain alpha-ketoacid dehydrogenase. These mutations cause the patients to accumulate high levels of the branched chain amino acids ("BCAA") leucine, isoleucine or valine that are neurotoxic and cause severe neurological pathologies characterized by brain edema, seizure, spasticity and respiratory irregularities that can lead to death. The MSUD name derives from the strong maple syrup odor in the urine of these patients. Similarly, IVA can result from a genetic defect leading to leucine accumulation. It is difficult to estimate the prevalence of these rare indications given few longitudinal studies. Based on estimates of the live birth rate of MSUD of 1:185,000 and IVA of 1:250,000, respectively, and applying assumptions to account for mortality and survival rates, it is estimated that there may be approximately 2,500 MSUD or IVA patients in the United States.

Currently available treatments for disorders involving the catabolism of BCAA are inadequate for the long-term management of the disorders and have severe limitations. A low protein/BCAA-restricted diet, with micronutrient and vitamin supplementation as necessary, is the widely-accepted long-term disease management strategy. However, BCAA-intake restrictions can be problematic since these amino acids are also essential nutrients that can only be acquired through diet and are necessary for metabolic activities such as protein synthesis. Even with proper monitoring and patient compliance, branched chain amino acid dietary restrictions result in a high incidence of mental retardation and mortality. MSUD is cured by liver transplantation; however, limited availability of donor organs, costs, and the need to rely on life-long immunosuppressant therapy are limiting. Therefore, there is significant unmet need for an effective, reliable, and/or long-term treatment for disorders involving the catabolism of branched chain amino acids.

We have built a Synthetic Biotic discovery program to modulate the expression of two BCAA transporters and three BCAA-degrading enzymes. Results *in vitro* demonstrate the efficient degradation of BCAAs into non-toxic branched-chain alcohols that can then be further metabolized and eliminated from the body. In preliminary studies in a mouse model of MSUD, the oral delivery of the Synthetic Biotic strain suppresses the increase in blood BCAA levels induced by a high-protein diet and prevents the associated waning, or moribund, phenotype as measured by improved locomotor activity. Based on the *in vivo* therapeutic effects observed, we continue to investigate this approach as a potential promising therapy for MSUD and IVA patients.

Our Synthetic Biotic Program for Propionic Acidemia and Methylmalonic Acidemia

Organic acidemias are a group of rare IEMs in which amino acid metabolism is disrupted, causing an accumulation of toxins. Normally, the human body converts certain amino acids, such as isoleucine, valine, threonine, and methionine, into a derivative of propionic acid to create energy. Patients with PA and MMA have enzyme deficiencies caused by mutations in the pathway for propionate catabolism that lead to the toxic accumulation of propionic acid or methylmalonic acid-related metabolites in the blood stream, leading to damage of the brain, heart, and liver. Clinical manifestations of the disease vary depending on the degree of enzyme deficiency and include seizures, vomiting, lethargy, hypotonia, encephalopathy, developmental delay, failure to thrive, and secondary hyperammonemia. It is difficult to estimate the prevalence of these indications given few longitudinal studies. The estimated live birth rates are 1:105,000-1:130,000 for PA and 1:50,000-100,000 for MMA. Applying assumptions to account for mortality and survival rates, it is estimated that there may be 2,000-3,000 PA or MMA patients in the United States.

Currently available treatments for disorders involving propionate catabolism are inadequate and have severe limitations. Patients may present acutely at birth with metabolic acidosis and hyperammonemia, or later in life with more heterogeneous clinical symptoms, and run the risk of early death or severe neurologic damage. Cognitive outcomes tend to be worse in PA, and patients who can also experience late complications like cardiomyopathy. Late complications for MMA patients include chronic kidney disease. Except for MMA patients who are responsive to vitamin B12, there is significant unmet need for effective, reliable and/or long-term treatment for disorders involving the catabolism of propionate.

Propionate is produced naturally in the gut by bacterial metabolism, and therefore a Synthetic Biotic medicine that consumes propionate in that environment could be an attractive approach to treating these

disorders. We have constructed discovery-stage Synthetic Biotic strains that have demonstrated degradation of propionate into non-toxic metabolites in vitro. In preliminary studies in a mouse model of propionic acidemia, the oral delivery of both Synthetic Biotic strains independently suppressed the plasma concentration of disease-related toxic metabolites. We plan to continue assessing these strains in animal models as potential promising therapies for PA and MMA patients.

Synthetic Biotic Medicines for Broader Metabolic Disease

Our Synthetic Biotic platform combined with our product discovery and development capabilities drive the potential for multiple clinically meaningful opportunities for patients affected by a broad set of metabolic diseases such as Nonalcoholic Steatohepatitis ("NASH"). For these indications, there is need for a safe, oral therapy with local activity in the gut to reset a metabolic dysfunction. Our approach is amenable to enabling combination therapy, which is increasingly recognized as a necessary component of effective treatment. We continue to explore strategic partnerships that would leverage the complementary capabilities of partners in order to develop Synthetic Biotic medicines for these broader groups of patients in need.

Synthetic Biotic Medicines for Immunomodulation

Our Synthetic Biotic platform has the potential to generate clinically meaningful therapies for patients affected by immune-mediated diseases. Among these conditions, IBD is particularly attractive, as it allows us to leverage knowledge and expertise gleaned from our metabolic programs to develop living medicines that can act locally at the site of disease in the gut. Because our approach is based on local delivery to the site of inflammation and not on systemic administration, we anticipate that our Synthetic Biotic medicines may offer an attractive safety profile in this setting. In 2015, we entered into a multi-year global collaboration with AbbVie focused on the discovery and development of a Synthetic Biotic medicines for the treatment of IBD.

Our Synthetic Biotic Medicines for Inflammatory Bowel Disease

IBD is a group of diseases characterized by significant local inflammation in the GI tract typically driven by T cells, activated macrophages and compromised function of the epithelial barrier. IBD pathogenesis is linked to both genetic and environmental factors and may be caused by altered interactions between gut microbes and the intestinal immune system. Current approaches to treat IBD are focused on therapeutics that modulate the immune system and suppress inflammation. These therapies include steroids, such as prednisone, and tumor necrosis factor inhibitors, such as Humira® (adalimumab). However, these approaches are associated with systemic immunosuppression, which includes greater susceptibility to infectious diseases and cancer. It is estimated that between 1.0-1.3 million patients have IBD in the United States.

Compromised gut barrier function also plays a central role in autoimmune diseases pathogenesis. A single layer of epithelial cells separates the luminal contents of the gut from the host circulatory system and the immune cells in the body. Disrupting the epithelial layer can lead to pathological exposure of foreign antigens from the lumen resulting in increased susceptibility to autoimmune disorders. The interplay between the gut microbiota and the host is thought to play key roles in both the maintenance of the epithelial barrier as well as homeostatic immunity. Thus, enhancing barrier function and reducing inflammation in the gastrointestinal tract are potential therapeutic mechanisms for the treatment or prevention of autoimmune disorders. Our Synthetic Biotic platform allows for the effective programming of *E. coli* Nissle to execute these functions, including the metabolic production of factors such short chain fatty acids to enhance barrier function and secreting proteins, such as immunomodulatory cytokines.

Our Synthetic Biotic Medicines for Immuno-Oncology

We believe boosting the body's immune response against tumor cells is one of the most promising advances in the treatment of cancer. The so-called "hot tumors", those with robust immune cell infiltration, specifically by

T cells, respond well to immunotherapies such as the PD-1 and CTLA-4 checkpoint inhibitors. Checkpoint inhibitors work by blocking pathways that inhibit T cells thus enabling them to recognize and destroy the tumor. Checkpoint inhibitors have significantly extended the lives of patients with several cancer types and, in some cases, have resulted in complete clinical responses. However, a large proportion of tumors are "cold" (i.e., they lack T cells), and respond poorly to immunotherapy.

Our goal is to leverage our Synthetic Biotic platform to design living medicines that can modify the tumor microenvironment to convert "cold" tumors into "hot." We believe that this transition will dramatically expand the patient population amenable to clinical benefit by immunotherapy. Our approach is designed to deliver robust therapeutic combinations to the tumors, without significant systemic exposure. Synthetic Biotic medicines are being developed to be administered by an intra-tumor injection or, in the case of GI cancers, by oral administration and can be engineered to perform three types of functions: metabolic conversions, secretions of proteins or bacterial surface display of specific single chain antibody domains, known as scFvs.

Our Synthetic Biotic platform allows it to approach "cold" tumors in a rational, mechanistic way, and can deliver multiple validated mechanisms to elicit specific immune responses in the tumor microenvironment. Our main mechanistic areas of focus in the context of tumor immunology include:

- *Immune activation and priming:* Our bacterial Synthetic Biotic chassis is predicted to engage innate immune cells in the tumor microenvironment, thereby initiating an immune cascade to activate and direct T cells to the tumor. Lack of effective presentation of tumor-specific antigens to T cells is recognized as a significant limitation to the initiation of immune responses in tumors. We are building and optimizing Synthetic Biotics medicines with the potential of addressing this issue. For example, we have built Synthetic Biotic candidates that produce STING agonist and can activate innate cytokines and adaptive T-cell responses to drive tumor regression.
- *Immune augmentation/Reversal of immunosuppression:* We have developed strains that actively consume and transform immunosuppressive metabolites in the tumor microenvironment, with the goal of setting up a milieu conducive to immune activation and tumor destruction. For example, we have built Synthetic Biotic candidates that consume Kyneurinine to reprogram the tumor microenvironment to drive tumor necrosis and antigen release.
- *T cell expansion:* Tumor antigen-specific T cell expansion and prevention of exhaustion are recognized as key objectives for successful cancer immunotherapy. We are developing Synthetic Biotic medicines programs to secrete specific cytokines to promote T cell survival and expansion.
- *Stromal modulation:* The physical structure of tumors is receiving increasing attention as emerging data demonstrate its importance in orchestrating tumor growth, immune evasion and resistance to chemotherapy, such as in pancreatic ductal adenocarcinoma. Tumor-derived extracellular matrix proteins can limit the perfusion of drugs or antibodies, contributing to the remarkable resistance of this tumor type to therapy. We have developed strains that secrete active enzymes with the capacity to remodel extracellular matrix proteins to make the tumor more permeable.

Our product vision for immuno-oncology is to use a rational approach to selecting and combining relevant mechanisms of action for the microenvironment of specific tumor types. For example, in animal models we are evaluating Synthetic Biotic medicines that combine the antigen release, activation and priming activities of a STING agonist with immune augmentation and T cell expansion of Kyneurine consumption and in early studies with intratumoral administration, in preclinical mouse models, we have observed high rates of durable response with an abscopal effect while avoiding systemic toxicity.

Collaboration Agreements

To accelerate the development and commercialization of Synthetic Biotic medicines to patients in therapeutic areas outside of IEMs, we have formed, and intend to seek other opportunities to form, strategic

alliances with collaborators that can expand our pipeline of therapeutic development and product candidates. We also work, and intend to seek additional opportunities to work, with multiple academic, research and translational medicine organizations and entities to deepen our understanding and development of living medicines with the potential to treat disease and disorders.

AbbVie

In July 2015, we entered into a license agreement with our subsidiary Synlogic IBDCo, Inc. ("IBDCo") and an Agreement and Plan of Merger with AbbVie (together, the "AbbVie Agreements") to collaborate on the discovery and development of Synthetic Biotic medicines for the treatment of IBD. The AbbVie Agreements provide AbbVie with an exclusive option to acquire IBDCo, which would then have an exclusive worldwide license to develop and commercialize up to three specified Synthetic Biotic medicines for the treatment of IBD.

Under the terms of the collaboration with AbbVie, we have the responsibility to discover, characterize and optimize one lead Synthetic Biotic product candidate to the point of a IND-enabling package, together with two backup product candidates, through a research and development program covering a limited number of effectors that modulate the IBD pathophysiology. The multi-year collaboration combines AbbVie's expertise in inflammatory diseases with our expertise in synthetic biology and metabolic engineering. AbbVie agreed to pay IBDCo an upfront payment of $2.0 million, received in December 2015, and up to $16.5 million upon the achievement of certain research and development milestones. In May 2017, IBDCo achieved one of these research and development milestones under the AbbVie Agreement for which it received $2.0 million.

If AbbVie accepts our IND-enabling package covering the lead Synthetic Biotic product candidate, AbbVie may exercise its exclusive option to acquire IBDCo, which would house the lead and two backup product candidates. If this option is exercised, AbbVie would pay us an option exercise fee upon the closing of the IBDCo merger and we would be eligible to receive future development, regulatory and commercial milestone payments, and low single digit royalties on sales of the Synthetic Biotic medicines. In addition, AbbVie would then assume full control of all further clinical development and commercial activity, including responsibility for all expenses and decisions.

Potential Future Collaborations

We view strategic partnerships as important drivers for helping accelerate our goal of effectively treating patients, and we will continue to seek strategic alliances with collaborators who can help fund, develop and commercialize our novel therapeutic development and product candidates, particularly in large metabolic indications and immuno-oncology. As the potential application of our Synthetic Biotics platform is extremely broad, we also plan to continue to identify academic, research and translational medicine organizations and entities that can contribute expertise and resources to our programs, to allow us to more rapidly expand our impact to broader patient populations.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from our collaborators or other third parties. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of synthetic biology. We additionally rely on data exclusivity, market exclusivity, and patent term extensions when available, and plan to seek and rely on regulatory protection afforded through orphan drug designations. Our commercial

success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned by third parties; to defend and enforce our proprietary rights, including our patents; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

We believe we are well positioned in terms of intellectual property because we:

- have built and expanded, and intend to continue expansion in, a broad worldwide portfolio of intellectual property, including patents and patent applications, in areas relevant to the development, manufacturing and formulation of human therapeutic products using live biotherapeutics based on synthetic biology;
- intend to take additional steps, where appropriate, to further protect our intellectual property rights, including, for example, through the use of copyright and trademark protection, as well as regulatory protection available via orphan drug designations, data exclusivity, market exclusivity and patent term extensions.

We believe our intellectual property portfolio provides broad coverage of our Synthetic Biotic platform and applicable disease-related technologies, which are directed to diseases and conditions associated with hyperammonemia, hyperphenylalanemia, other IEMs and acquired metabolic disorders, autoimmune and other inflammatory disorders and oncology. As of January 22, 2018, we had 143 Synlogic-owned and in-licensed patents and patent applications in U.S. and foreign jurisdictions, including 20 issued and allowed patents.

Disease-related applications.

The disease-related applications in our intellectual property portfolio relate to certain pathological conditions and provide coverage for engineered bacteria having genetic circuitry designed to specifically address those conditions and the associated disease states. Disease related applications relate to pathological conditions and include:

Hyperammonemia

- Our lead program addresses conditions associated with hyperammonemia, for which we have developed engineered bacterial strains containing genetic circuitry specifically designed to metabolize ammonia.
- The intellectual property portfolio provides coverage for compositions directed to engineered bacterial strains, methods of making the bacterial strains and methods for treating diseases that involve accumulation of ammonia (e.g., UCD, HE). Our intellectual property provides coverage for the lead product candidate SYNB1020 and methods of its manufacture and use. In addition to UCD, SYNB1020 could be useful for the treatment of hyperammonemia in HE patients with cirrhosis of the liver, which indication is also covered by our intellectual property.
- Currently, intellectual property relating to this technology includes 19 pending applications in U.S. and foreign jurisdictions, as well as two issued U.S. patents directed to composition of matter and pharmaceutical composition claims covering our clinical candidate. The patent term for this IP will expire in December 2035, excluding any patent term adjustments or extensions.

Hyperphenylalanemia

- Our program addresses conditions associated with hyperphenylalanemia, for which we have developed engineered bacterial strains containing genetic circuitry specifically designed to metabolize phenylalanine.

- Our intellectual property portfolio provides coverage for compositions directed to engineered bacterial strains, methods of making the bacterial strains and methods for treating diseases that involve accumulation of phenylalanine. Our intellectual property provides coverage for the lead product candidate SYNB1618 and methods of its manufacture and use.
- Currently, intellectual property relating to this technology includes nine pending U.S. patent applications as well as two allowed U.S. patents and 10 international patent applications directed to composition of matter and pharmaceutical compositions covering our lead product candidate. The patent term for this intellectual property will expire in May 2036, excluding any patent term adjustments or extensions.

Other Inborn Errors of Metabolism

- Additional disease-related intellectual property includes patent applications directed to our Synthetic Biotic technology for use in treating diseases and conditions arising from IEMs.
- Our intellectual property provides coverage of compositions of engineered bacteria, methods of making the bacterial strains and methods of treating diseases associated with accumulation of BCAA (e.g., leucine, isoleucine and valine), including MSUD. We currently have three U.S. applications and five international applications directed to diseases involving accumulation of BCAA. The patent term for this intellectual property will expire in June 2036, excluding any patent term adjustments or extensions.
- Our additional intellectual property covers compositions of engineered bacteria, methods of making the bacterial strains and methods of treating organic acidemias, including those associated with accumulation of propionic acid and related toxic metabolites, such as PA and MMA. We currently have one U.S. application and one PCT application directed to diseases involving accumulation of organic acid metabolites. The patent term for this intellectual property will expire in July 2036, excluding any patent term adjustments or extensions.

Metabolic Disorders

- In addition to IEMs, other disease-related intellectual property includes patent applications directed to our Synthetic Biotic technology for use in treating diseases and conditions associated with acquired metabolic disorders, including, but not limited to NASH.
- Our intellectual property provides broad coverage of compositions of engineered bacteria, methods of making the bacterial strains and methods of treating various metabolic diseases. Our current intellectual property consists of one U.S. application and four international applications relating to this technology. The patent term for this intellectual property has expiration dates ranging from June 2036 to December 2036, excluding any patent term adjustments or extensions.

Inflammatory and Autoimmune Diseases

- Additional disease-related intellectual property includes numerous patent applications directed to our Synthetic Biotic technology for use in treating diseases and conditions associated with an inflammatory state, including, but not limited to, diseases associated with gut inflammation, compromised gut mucosal barrier (leaky gut), and various autoimmune disorders.
- Our intellectual property provides broad coverage of compositions of engineered bacteria, methods of making the bacterial strains and methods of treating diseases associated with gut inflammation, leaky gut, and autoimmune disorders, such as Inflammatory Bowel Disease, including Crohn’s Disease, ulcerative colitis, and other diseases. Our current intellectual property consists of seven U.S. applications and 14 international applications relating to this technology, which is being developed in collaboration with AbbVie and which intellectual property is Synlogic-owned. The patent term for this

intellectual property has expiration dates ranging from December 2035 to March 2036, excluding any patent term adjustments or extensions. In addition, we have has one U.S. application and five international applications relating to this technology which is jointly owned by us and MIT, which expires in December 2035, excluding any patent term adjustments or extensions.

Immuno-Oncology

- In addition, we have disease-related intellectual property directed to our Synthetic Biotic technology for use in immuno-oncology, which intellectual property covers bacterial strains engineered to metabolize and/or produce biomolecules that modify the tumor microenvironment and immune response, resulting in an array of mechanistic functions, including immune activation and priming, immune augmentation and/or reversal of immunosuppression, T-cell expansion, and tumor stromal modulation.
- Our intellectual property provides broad coverage of compositions of engineered bacteria, methods of making the bacterial strains and methods of treating various cancers. Our current intellectual property consists of two PCT applications and five U.S. applications with expiration dates ranging from January 2037 to February 2037, excluding any patent term adjustments or extensions.

Platform Technology Applications.

In addition to the disease-related technology, our intellectual property portfolio also includes applications directed to platform technologies developed internally by us. Exemplary platform technologies include bacterial chassis-related and genetic circuitry-related technological developments, including, for example, improvements in inducible gene regulation, control of bacterial cell growth, including auto-regulation thereof, and systems for importing metabolites, as well as secreting therapeutic effectors. These platform technologies, and our intellectual property coverage thereof, are broadly applicable to our therapeutic Synthetic Biotic medicines.

In addition to our own patent applications, we have licensed patents and patent applications from MIT and Trustees of Boston University (“BU”) to access intellectual property covering synthetic biology circuitry that we are exploring and developing. The intellectual property licensed from MIT and BU relates to genetic circuitry (designed to be modular components for integration into biological systems), cells containing the genetic circuitry, and methods and systems for gene regulation using the genetic circuitry.

The intellectual property licensed from MIT includes applications related to genome editing systems used to target specific genes for recombination and methods for delivering a gene editing system to endogenous bacteria. It also includes applications directed to genetic circuits and biological systems for regulating gene expression using various recombinase-based and other promoter systems, including promoter systems that respond to different levels of an input signal. The MIT intellectual property also covers methods for identifying mutant promoters that have an altered level of response to an input signal and methods of controlling gene expression in certain bacteria. In addition, the MIT intellectual property includes a PCT application jointly owned by us and MIT, directed to engineered bacteria and methods for treating inflammatory bowel disease. The licensed patents and applications from the MIT have expiration dates ranging from 2033 to 2037, excluding any patent term adjustments or extensions.

The intellectual property licensed from BU includes patents and applications relates to genetic circuitry and biological systems for controlling gene expression employing the genetic circuits, detecting the production of a target gene product, and delivering genetic circuits to endogenous bacteria. The various genetic circuits are designed to respond to external cues and also designed to tighten control of gene expression regulated by inducible and constitutive promoter systems using a variety of genetic components, for example, sensors, inducers, repressors, antisense, stem-loop sequences, recombinases, RNAi, inverted sequences, and ribosome-binding site sequences, to generate various promoter toggle switches, adjustable threshold switches, and

oscillator switches, among others. In addition, the BU intellectual property covers biocontainment systems that couple environmental sensing with circuit-based control of cell viability. The licensed patents and applications from BU have expiration dates ranging from 2019 to 2036, excluding any patent term adjustments or extensions.

Massachusetts Institute of Technology ("MIT") License

We entered into a license agreement with MIT, effective November 2015 and amended as of July 2016. Under this license agreement, MIT granted us a worldwide license under certain patents and patent applications that is exclusive in the therapeutics and theranostics fields and non-exclusive in the internal research field. The license grants us rights to develop, make, have made, use, import, sell, and offer to sell licensed products and processes. We do not have the right to control prosecution of these licensed patents and patent applications and our rights to enforce the in-licensed patent rights are subject to certain limitations.

Under the terms of the MIT license agreement, as consideration for the license, we paid to MIT an upfront license fee and are eligible to receive an annual maintenance fee, milestone fees, sublicense fees if we should ever grant a sublicense to the licensed patents or patent applications and low single-digit royalty percentages on net sales of licensed products. MIT also receives reimbursement from us for patent prosecution expenses. We are subject to diligence requirements to develop licensed products in accordance with certain development milestones.

BU and MIT License

We entered into a license agreement with BU and MIT effective October 2015 and signed April 2017. Howard Hughes Medical Institute ("HHMI") has an ownership interest in certain patent rights licensed to us under this license, which interest HHMI assigned to BU. HHMI is not a party to the license agreement, but receives the benefit of certain terms. Under this license agreement, BU and MIT granted us a worldwide license under certain patents and patent applications that is exclusive in the therapeutics and theranostics fields and non-exclusive in the diagnostic and internal research field. The license grants us rights to make, have made, use, lease, import, sell, and offer to sell licensed products and processes. We do not have the right to control prosecution of the licensed patents and patent applications, and our rights to enforce the licensed patent rights are subject to certain limitations. Under the terms of this license agreement, as partial consideration for the license, BU, MIT and MIT's agent Omega Cambridge SPV, L.P. were issued an aggregate of 325,377 shares of our common stock. In addition, we paid an upfront fee, and reimbursed past patent prosecution costs, and the licensors are eligible to receive from us an annual maintenance fee, milestone fees, sublicense fees if we should ever grant a sublicense to the licensed patents and patent applications and low single-digit royalty percentages on net sales of licensed products. BU also receives reimbursement from us for patent prosecution expenses. We are subject to diligence requirements to develop licensed products in accordance with certain development milestones.

Individual patents extend for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States are effective for 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to account for delays in prosecution at the U.S. Patent and Trademark Office and/or to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. For regulatory delays, the restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective non-provisional filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

The patent positions of companies like us are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of synthetic biology has emerged in the United States. The patent situation outside of the United States is even more uncertain. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us the future will be commercially useful in protecting our products and the methods used to manufacture those products. For additional risks, please see the section entitled "*Risk Factors—Risks Related to Intellectual Property*" in this prospectus supplement.

Trademarks

Our registered trademark portfolio currently contains six registered trademarks, five pending trademark applications in the United States and four pending trademark applications in Canada and India under the Madrid Protocol.

Other

Generally, we seek to protect our technology and product candidates, in part, by entering into confidentiality agreements with those who have access to our confidential information, including employees, contractors, consultants, collaborators, and advisors. In some circumstances, we may rely on trade secrets to protect our technology. We seek to preserve the integrity and confidentiality of our proprietary technology, trade secrets and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or may be independently discovered by competitors. To the extent that company employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For this and more comprehensive risks related to our proprietary technology, inventions, improvements and products, please see the section entitled " *Risk Factors—Risks Related to Intellectual Property,* " in this prospectus supplement.

Regulatory Matters

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the NDA process and a new biologic must be approved by the FDA through the biologics license application ("BLA"), process before it may be legally marketed in the United States

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and in the case of biologics, also under the Public Health Service Act ("PHSA"), and implementing regulations. Our product candidates will be regulated by the FDA as biologics. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to

approve pending applications, withdrawal of an approval, license revocation, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to GLP other applicable regulations;
- submission to the FDA of an investigational new drug application ("IND") which must become effective before human clinical trials may begin;
- performance of adequate and well controlled human clinical trials according to GCP to establish the safety and efficacy of the proposed drug for its intended use;
- development and approval of a companion diagnostic device if the FDA or the sponsor believes that its use is essential for the safe and effective use of a corresponding product;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the BLA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. In June 2016, the FDA issued an updated guidance for the industry entitled "Early Clinical Trials with Live Biotherapeutic Products: Chemistry, Manufacturing and Control Information," which included recommendations from the FDA regarding the chemistry, manufacturing and control information that should be included in an IND for early clinical trials with live biotheraeutic products. Guidances such as this one reflect the FDA's thinking on a topic at the time that they are issued and although this guidance is not binding on the FDA or a sponsor, it provided us with additional information about what should be included in our IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about ongoing or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP requirements. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An institutional review board ("IRB") at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a BLA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. Phase 1, Phase 2, and Phase 3 testing may not be completed successfully within any specified period, if at all.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before a BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug. If this type of discussion occurs, a sponsor may be able to request a Special Protocol Assessment ("SPA"), the purpose of which is to reach agreement with the FDA on the design of the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

According to FDA guidance for industry on the SPA process, a sponsor that meets the prerequisites may make a specific request for a special protocol assessment and provide information regarding the design and size of the proposed clinical trial. The FDA is required to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began. If the sponsor makes any unilateral changes to the approved protocol, the agreement will be invalidated.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for

manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. However, there are evolving rules and increasing requirements for publication of all trial related information, and it is possible that data and other information from trials involving drugs that never garner approval could require disclosure in the future.

U.S. Review and Approval Processes

The results of product development, preclinical and other nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling, and other relevant information are submitted to the FDA as part of a BLA requesting approval to market the product. The submission of a BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances, including where the biologic has been designated as an orphan drug. The user fee for FY 2018 is $2,241,495 for an application containing clinical data. The FDA reviews all BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept a BLA for filing. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in depth substantive review. FDA may refer the BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve a BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA may issue a complete response letter, which may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the BLA, or an approved letter following satisfactory completion of all aspects of the review process. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving a BLA, the FDA will inspect the facility or facilities where the product is manufactured.

BLAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. Priority review for an original BLA

will be six months from the date that the BLA is filed. In addition, products studied for their safety and effectiveness in treating serious or life threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well controlled Phase 4 clinical trials. Priority review and accelerated approval do not change the standards for approval, but may expedite the approval process.

After the FDA evaluates a BLA, it will issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. A CRL usually describes the specific deficiencies in the BLA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a CRL is issued, the sponsor must resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the BLA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness after BLA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a Risk Evaluation and Mitigation Strategy ("REMS"), to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

The Pediatric Research Equity Act ("PREA"), requires a sponsor to conduct pediatric clinical trials for most drugs and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original BLAs and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. Orphan indications are exempt from PREA. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (referred to as the "Hatch Waxman Amendments"). The Hatch Waxman Amendments permit a

patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one half the time between the effective date of an IND, and the submission date of a BLA, plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of its currently-owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the filing of the relevant NDA.

Pediatric exclusivity is a type of marketing exclusivity available in the United States. Under the Best Pharmaceuticals for Children Act (the "BPCA"), an additional six months of marketing exclusivity may be available if a sponsor conducts clinical trials in children in response to a written request from the FDA. If a written request does not include clinical trials in neonates, the FDA is required to include its rationale for not requesting those clinical trials. The FDA may request studies on approved or unapproved indications in separate written requests. The issuance of a written request does not require the sponsor to undertake the described clinical trials. To date, we have not received any written requests.

Biologics Price Competition and Innovation Act of 2009

The ACA, which included the BPCIA, amended the PHSA to create an abbreviated approval pathway for two types of "generic" biologics, biosimilars and interchangeable biologic products, and provides for a 12-year data exclusivity period for the first approved biological product, or reference product, against which a biosimilar or interchangeable application is evaluated; however if pediatric clinical trials are performed and accepted by the FDA, the 12-year data exclusivity period will be extended for an additional six months. Because our product candidates will be regulated as biologics, if they are approved they may be subject to competition from biosimilars. A biosimilar product is defined as one that is highly similar to a reference product notwithstanding minor differences in clinically-inactive components and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. An interchangeable product is a biosimilar product that may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

The biosimilar applicant must demonstrate that the product is biosimilar based on data from (1) analytical studies showing that the biosimilar product is highly similar to the reference product; (2) animal studies (including toxicity); and (3) one or more clinical trials to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

An application for a biosimilar product may not be submitted until four years after the date on which the reference product was first approved. The first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed, but the exclusivity period may be shortened under certain circumstances.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease

or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use will be disclosed publicly by the FDA; the posting will also indicate whether a drug is no longer designated as an orphan drug. More than one product candidate may receive an orphan drug designation for the same indication. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to seven years of orphan product exclusivity, except in very limited circumstances. The FDA will not recognize orphan drug exclusive approval if a sponsor fails to demonstrate upon approval that the drug is clinically superior to a previously approved drug, regardless of whether or not the approved drug was designated an orphan drug or had orphan drug exclusivity. Thus orphan drug exclusivity could also block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA and we are not able to show the clinical superiority of our drug or if our product candidate is determined to be contained within the competitor's product for the same indication or disease.

In August 2016, the FDA granted us orphan drug designation for our lead product candidate *E. coli* Nissle bacterium modified to metabolize ammonia for the treatment of urea cycle disorders. In October 2017, the FDA granted SYNB1618 orphan drug designation for PKU. Orphan drug designation will provide us with seven years of market exclusivity that begins when the BLA for the drug receives FDA marketing approval for the use for which the orphan drug status was granted.

Expedited Review and Approval

The FDA has various programs, including Fast-Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast-Track is a process designed to facilitate the development, and expedite the review, of drugs to treat serious diseases and fill an unmet medical need. The request may be made at the time of IND submission and generally no later than the pre-BLA meeting. The FDA will respond within 60 calendar days of receipt of the request. Priority review, which is requested at the time of BLA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of 10 months. Although Fast-Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast-Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides an earlier approval of drugs that treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. Discussions with the FDA about the feasibility of an accelerated approval typically begin early in the development of the drug in order to identify, among other things, an appropriate endpoint. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing clinical trials to confirm the appropriateness of the surrogate marker trial.

A Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint. A sponsor may request Breakthrough Therapy designation at the time that the IND is submitted, or no later than at the end of Phase 2 meeting. The FDA will respond to a Breakthrough Therapy designation request within 60 days of receipt of the

request. A drug that receives Breakthrough Therapy designation is eligible for all Fast-Track designation features, intensive guidance on an efficient drug development program, beginning as early as Phase 1 and commitment from the FDA involving senior managers.

In June 2017, the FDA granted us Fast-Track designation for the use of a genetically modified strain of *E. coli* Nissle, SYNB1020, for the treatment of urea cycle disorders.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws and regulations. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

Any drug products manufactured or distributed by us or our partners pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label.

From time-to-time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency where it will be

evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan designated product.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third party reimbursement. Third party payors include government healthcare programs such as Medicare, managed care providers, private health insurers and other organizations. We anticipate third party payors will provide reimbursement for our products. However, these third party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly-approved healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of our products. Our product candidates may not be considered cost effective. It is time consuming and expensive for us to seek reimbursement from third party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

Medicare is a federal healthcare program administered by the federal government that covers individuals age 65 and over as well as individuals with certain disabilities. Drugs may be covered under one or more sections of Medicare depending on the nature of the drug and the conditions associated with and site of administration. For example, under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage for outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level.

Medicare Part B covers most injectable drugs given in an in-patient setting and some drugs administered by a licensed medical provider in hospital outpatient departments and doctors' offices. Medicare Part B is administered by Medicare Administrative Contractors, which generally have the responsibility of making coverage decisions. Subject to certain payment adjustments and limits, Medicare generally pays for a Part B-covered drug based on a percentage of manufacturer-reported average sales price, which is regularly updated. We believe that our product candidates that are intended to be administered intratumorally will be subject to the Medicare Part B rules.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of healthcare costs, including the cost of prescription drugs. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, "ACA") enacted in March 2010, was expected to have a significant impact on the health care industry. The ACA has been under scrutiny by the U.S. Congress almost since its passage, and certain sections of the ACA have not been fully implemented or effectively repealed. As a result, its longevity continues to be uncertain. In addition, ongoing initiatives in the U.S. have increased and will continue to increase pressure on drug pricing. The announcement or adoption of any such initiative could have an adverse effect on potential revenues from any product candidate that we may successfully develop.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on our profitability placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Other Regulatory Matters

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. These operations may involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations may also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes.

Manufacturing

We have made and continue to make significant investments to develop manufacturing processes designed to allow it to reproducibly manufacture high quality living medicines at clinical scale and, later, at commercial scale to enable approval of our product candidates. We have a small-scale internal development group to support discovery and preclinical research and are building the organization to support scale-up and development towards commercialization. We currently work with contract manufacturing organizations ("CMOs") for clinical material and formulation development work.

We have successfully transferred our manufacturing process for our lead hyperammonemia and our PKU programs to a CMO where it was used to manufacture Phase 1 clinical material pursuant to FDA's cGMP requirements.

We have successfully transferred our manufacturing process for our lead hyperammonemia program to a CMO where it was used to manufacture Phase 1 clinical material pursuant to FDA's cGMP requirements.

These first clinical materials use a liquid formulation. We are investing in formulation development in parallel with Phase 1 clinical trial progress with the goal of providing a solid dose oral formulation (tablets or capsules) for later stage clinical development and commercial presentation, likely with a sachet formulation for pediatric use.

To enable the production of high levels of cells, or biomass, that can be administered as activated living medicines to perform metabolic functions, we can engineer our Synthetic Biotic medicines with switches. These

switches are comprised of transcription factor and promoter pairs that allow for controlled expression of the therapeutic effectors produced by our Synthetic Biotic medicines. To ensure the metabolic capacity of the cells is allotted to the production of a high level of biomass during manufacturing, the effector circuits in the Synthetic Biotic programs are not expressed during this growth phase. At the end of the manufacturing process, the circuits are then induced, or activated. This two-step approach was designed to enable a high level of biomass production as well as to deliver the required activity necessary at the time of administration.

As we progress in clinical development, we will need to scale up from Phase 1 clinical-scale to commercial-scale manufacturing. We are in the process of assessing CMOs who meet our criteria to supply our later-stage clinical development and commercial supply. We plan to compare the merits of working with one or more CMOs who meet our criteria with the possibility of building cGMP manufacturing capacity and capabilities internally.

Competition

The biotechnology industry is extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in synthetic biology and metabolic engineering of probiotic bacteria, our clinical development expertise, and dominant intellectual property position, we currently face and will continue to face competition for our development programs from companies that use synthetic biology or cell therapy development platforms and from companies focused on more conventional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including larger pharmaceutical companies, biotechnology companies and academia. Many of these competitors may have access to greater capital and resources than us. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, in establishing clinical trial sites and patient registration for clinical trials, and in accessing technologies to enable our programs. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that may become available in the future.

Competitors to our efforts to provide living medicines to patients with a wide range of indications include other synthetic biology companies developing other synthetic biology methods, cellular and microbiome-based companies, DNA and RNA-based companies, as well as companies developing small molecules or other biologics. In the case of indications that we are targeting with our own Synthetic Biotic medicines, competitors include, but are not limited to:

- *UCD*
  - Horizon Pharma plc has a licensed product; and
  - Dimension Therapeutics, Inc. (currently in definitive agreement for acquisition by Ultragenyx Pharmaceutical Inc.), Aeglea Biotherapeutics, Inc., Arcturus Therapeutics Inc., Castle Creek Pharma LLC, PhaseRx, Inc., Translate Bio (formerly RaNA Therapeutics) and Selecta Biosciences, Inc. are each involved with discovery or pre-clinical stage product candidates.
- *HE*
  - Valeant Pharmaceuticals International, Inc. has a licensed product; and
  - Ocera Therapeutics, Inc. (recently acquired by Mallinckrodt Pharmaceuticals) , Umecrine Cognition AB and Salix Pharmaceuticals, Ltd, as well as other pre-clinical and discovery stage companies are each developing product candidates.
- *PKU*
  - BioMarin, Inc. has a licensed and development stage product; and
  - MipSalus ApS, Codexis, Inc., Dimension Therapeutics, Inc.(currently in definitive agreement for acquisition by Ultragenyx Pharmaceutical Inc.)and Synthetic Biologics, Inc. are each developing product candidates.

Our Team: Executives, Founders and Scientific Advisors

Our team of executives has proven track records of successfully translating scientific visions into successful commercial therapeutic products, solving complex issues in developing novel therapeutics and progressing new and novel products through regulatory approval. Our scientific founders, Timothy Lu, M.D., Ph.D., and James Collins, Ph.D., are experts in the emerging field of synthetic biology. In addition to our management team and founders, we have established advisory relationships with researchers and clinicians dedicated to the development of Synthetic Biotic therapeutic products for patients with significant unmet medical needs and whose expertise spans synthetic biology, metabolic engineering, metabolism, immuno-modulation and immuno-oncology arenas. Our scientific advisors include Dr. Lu and Dr. Collins; Christopher Voigt, Ph.D., Cammie Lesser, M.D., Ph.D. and Kristala Prather, Ph.D., experts in synthetic biology and bacterial metabolism; and Charles Mackay, Ph.D., Ulrich von Andrian, M.D., Ph.D. and Sangeeta Bhatia, M.D., Ph.D., experts in immunomodulation and oncology. We intend to expand our advisory boards as we grow. All of our founders and advisors are equity holders in us and receive compensation as scientific advisors. Although they are regularly available for scientific consultation, our arrangements with these individuals do not entitle us to any of their existing or future intellectual property derived from their independent research or research with other third parties.

Employees

As of January 1, 2018, we had 57 full-time employees, 32 of whom have an M.D. or Ph.D. Of our full-time employees, 42 were primarily engaged in research and development activities. None of our employees are subject to a collective bargaining agreement. We believe that we have good relations with our employees.

Facilities

We currently lease facilities at 200 Sidney Street, Suite 320, Cambridge, Massachusetts 02139 containing our research and development, laboratory and office spaces. This facility consists of approximately 14,390 square feet. Our lease expires in April 2021. In July 2017, we entered into an agreement to lease approximately 41,346 square feet of laboratory and office space in Cambridge, Massachusetts. Annual rent is approximately $3.1 million. The ten-year lease is estimated to commence in January 2018 and contains provisions for a free-rent period, annual rent increases and an allowance for tenant improvements. Additionally, we have committed to a tenant improvement investment of approximately $1.6 million. In conjunction with the lease, we established a letter of credit of approximately $1.0 million.

In July 2017, we entered into an agreement to terminate our existing lease of laboratory and office space in Cambridge, Massachusetts at a date that is 30 days after the commencement of our new lease. No penalties are associated with the termination of the lease.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Corporate Information and History

We were originally incorporated in the State of Delaware in December 2007 under the name “Mirna Therapeutics, Inc.” We carry on our business directly and through our subsidiaries.

Our subsidiary, Synlogic Operating Company, Inc. was incorporated in Delaware as TMC Therapeutics, Inc. on March 14, 2014. On July 15, 2014, TMC Therapeutics, Inc. changed its name to Synlogic, Inc. (“Private Synlogic” when referred to prior to the Merger (as defined below)). On July 2, 2015, the common and preferred shareholders of Private Synlogic executed the Synlogic, LLC Contribution Agreement, pursuant to which such

common and preferred shareholders contributed such shareholders' equity interests in Private Synlogic in exchange for common and preferred units in a newly formed parent company named Synlogic, LLC (the "2015 Reorganization"). In addition, IBDCo was formed as a subsidiary of Synlogic, LLC, as part of the 2015 Reorganization, and we entered into a license, option and merger agreement with AbbVie for the development of treatments for IBD. In May 2017, we completed a series of transactions pursuant to which Synlogic, LLC merged with and into Private Synlogic with Private Synlogic continuing as the surviving corporation.

On August 28, 2017, Synlogic, Inc., formerly known as Mirna Therapeutics, Inc. (NASDAQ: MIRN) ("Mirna"), completed its business combination with Synlogic, Inc. 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 25, 2017, in connection with, and prior to the completion of, the Merger, Mirna effected a 1:7 reverse stock split of its common stock (the "Reverse Stock Split"), and on August 28, 2017, immediately after completion of the Merger, Mirna changed its name to "Synlogic, Inc." (NASDAQ: SYBX).

Under the terms of the Merger Agreement, Mirna issued shares of its common stock to Private Synlogic's stockholders, at an exchange ratio of 0.5532 shares of Mirna's common stock, after taking into account the Reverse Stock Split, for each share of Private Synlogic common stock and preferred stock outstanding immediately prior to the Merger ("Merger Exchange Ratio"). The Merger Exchange Ratio was determined through arms'-length negotiations between Mirna and Private Synlogic. Mirna assumed all of the stock options outstanding under the Synlogic 2017 Stock Incentive Plan ("2017 Plan"), with such stock options henceforth representing the right to purchase a number of shares of Mirna's common stock equal to 0.5532 multiplied by the number of shares of Private Synlogic common stock previously represented by such options. Mirna also assumed the 2017 Plan.

Immediately after the Merger, there were 16,282,496 shares of our common stock outstanding. At this time, the former stockholders and optionholders of Private Synlogic owned, or held rights to acquire, approximately 82.4% of our fully-diluted common stock, which for these purposes is defined as our outstanding common stock , plus "in the money" options, assuming that all "in the money" options outstanding immediately prior to the Merger were exercised on a cashless basis immediately prior to the closing of the Merger (the "Fully-Diluted Common Stock"), with Mirna's stockholders and optionholders immediately prior to the Merger owning approximately 17.6% of our Fully-Diluted Common Stock.

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

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

Leerink Partners LLC and Piper Jaffray & Co. are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	
Piper Jaffray & Co.	
H.C. Wainwright & Co., LLC	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

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

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

Certain of our existing stockholders, who are affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $15 million in shares of common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares of common stock in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, fewer or no shares of common stock in this offering.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus 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 the offering may be changed by the representatives.

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 underwriters of their option to purchase additional shares of our common stock.

		Total	
	Per Share	Without Option	With Option
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 $250,000. We also have agreed to reimburse the underwriters for up to $25,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

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

No Sales of Similar Securities

We, our executive officers and directors and certain of our other existing security holders 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 without first obtaining the written consent of Leerink Partners LLC and Piper Jaffray & Co. on behalf of the underwriters. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock.

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 underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives 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 the offering, the underwriters 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 underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters 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 underwriters are 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 the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' 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 underwriters may conduct these transactions on the Nasdaq Capital Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters 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 nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

The underwriters 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 the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their 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. Some of the underwriters and certain of their 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 underwriters and their 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 underwriters and their 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 Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, 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 Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the representatives and each of our and the representatives' and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in Canada

The securities 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 securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (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 underwriters are 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 underwriters in connection with certain legal matters related to this offering.

EXPERTS

Ernst & Young LLP, predecessor independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

The consolidated financial statements of Synlogic, LLC at December 31, 2016 and 2015, and for the years then ended, 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 read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is *www.sec.gov*. 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, 2016, filed with the SEC on March 15, 2017;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 9, 2017;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, filed with the SEC on August 4, 2017
- our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, filed with the SEC on November 13, 2017
- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 27, 2017, but only to the extent incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2016;
- our Current Reports on Form 8-K or Form 8-K/A, as applicable, filed with the SEC on May 16, 2017, May 25, 2017, June 29, 2017, August 25, 2017, August 28, 2017, September 26, 2017, October 10, 2017, October 16, 2017, October 24, 2017 and November 8, 2017 (in each case, except for information contained therein which is furnished rather than filed); and
- 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: 200 Sidney Street, Cambridge, Massachusetts 02139, 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.

Table of Contents

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, rights or performance of purchase contracts; or any combination of these 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 October 12, 2017, the last reported sale price of our common stock was $16.43 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 October 25, 2017.

TABLE OF CONTENTS

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, rights or purchase contracts to purchase any of such 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, or the Merger, 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. Synlogic applies the principles and tools of synthetic biology to engineer beneficial probiotic bacteria to perform or deliver critical therapeutic functions, compensating for missing or damaged pathways in patients with these serious diseases. As living medicines, Synthetic Biotic medicines are designed to sense a local disease context within a patient's body and to respond by metabolizing toxic substances or delivering combinations of therapeutic factors.

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 19 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 200 Sidney Street, Cambridge, Massachusetts 02139 and our telephone number is (617) 401-9947. 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, rights or purchase contracts to purchase any of such 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, 2016, 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:

- our history of losses;
- the nature of our clinical-stage business and our requirements for substantial additional funding;
- our limited operating history;
- the costs, time and risks associated with our clinical trials;
- our novel and unproven approach to drug discovery and development, including our Synthetic Biotic product candidates;
- our efforts to expand our development platform to build a pipeline of product candidates;
- the potential for our product candidates to cause undesirable side effects or adverse events that could delay or prevent their regulatory approval or result in significant negative consequences after approval;
- our reliance on the success of our product candidates, none of which have completed clinical trials;
- our ability to obtain or maintain orphan drug exclusivity for some of our products;
- the uncertainty of outcomes for our product development and our clinical trials;
- delays or difficulties associated with the enrollment of patients;
- the possibility that we may incur substantial liability and costs if we face successful product liability claims;
- the challenges of obtaining and maintaining successful regulatory approval for our product candidates in a changing regulatory environment for healthcare providers and drug development companies;
- our ability to obtain and maintain intellectual property protection for our Synthetic Biotic targets, product candidates and processes for our development timeline;
- ethical, legal and social concerns about synthetic biology and genetic engineering;
- our ability to defend claims challenging the inventorship of our intellectual property and to protect our intellectual property rights around the world;

- our reliance on third parties to conduct some aspects of our research and development, manufacturing and supply;
- our collaborative arrangements or strategic alliances;
- our ability to successfully commercialize our product candidates and to achieve market acceptance;
- our ability to obtain or maintain adequate reimbursement or insurance coverage for our products, if any;
- our ability to attract and retain key scientific or management personnel;
- the volatility of our stock price;
- the marketability of our common stock; and
- our broad discretion to invest or spend the proceeds of our financings in ways with which our stockholders may not agree and may have limited ability to influence.

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 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

- 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 October 12, 2017, we had 16,282,496 shares of common stock outstanding and approximately 156 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;
- 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;

- 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

- 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 depositary 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, will we 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 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, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
- any applicable material U.S. federal income tax considerations; and
- whether the purchase contracts will be issued in fully registered or global form.

The preceding description sets forth certain general terms and provisions of the purchase contracts to which any prospectus supplement may relate. The particular terms of the purchase contracts to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the purchase contracts so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the purchase contracts described in a prospectus supplement differ from any of the terms described above, then the terms described above will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable purchase contract for additional information before you decide whether to purchase any of our purchase contracts.

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, rights or purchase contracts for the purchase of common stock, preferred stock and/or debt securities in one or more series, 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 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 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

Ernst & Young LLP, predecessor independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

The consolidated financial statements of Synlogic, LLC at December 31, 2016 and 2015, and for the years then ended, 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 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, 2016 that we filed with the SEC on March 15, 2017;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017 and June 30, 2017 that we filed with the SEC on May 9, 2017 and August 4, 2017, respectively;
- our Current Reports on Form 8-K or Form 8-K/A that we filed with the SEC, as applicable, on May 16, 2017, May 25, 2017, June 29, 2017, August 25, 2017, August 28, 2017, September 26, 2017 and October 10, 2017 (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.
200 Sidney Street, Suite 320
Cambridge, Massachusetts 02139
Attention: Investor Relations
Telephone: (617) 401-9947

You may also access these documents on our website, *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

Joint Book-Running Managers

Leerink Partners **Piper Jaffray**

Lead Manager

H.C. Wainwright & Co.

, 2018