UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2018

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-37566

SYNLOGIC, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**26-1824804**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
301 Binney St., Suite 402 Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 401-9975

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.001 per share	**Nasdaq Capital Market**

Securities registered pursuant to Section 12(g) of The Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Small reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of common stock held by non-affiliates of the registrant as of June 30, 2018, the last business day of the registrant's most recently completed second quarter, was $174.8 million, computed based on the closing price of $9.83 per share on June 30, 2018.

As of March 5, 2019 there were 25,400,495 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the registrant's definitive proxy statement for the 2019 annual meeting of stockholders to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2018.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained herein are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the success of our research and development efforts;
- the initiation, progress, timing, costs and results of clinical trials for our product candidates;
- the time and costs involved in obtaining regulatory approvals for our product candidates;
- the progress, timing and costs involved in developing manufacturing processes and agreements with third-party manufacturers;
- the rate of progress and cost of our commercialization activities;
- the expenses we incur in marketing and selling our product candidates;
- the revenue generated by sales of our product candidates;
- the emergence of competing or complementary technological developments;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish;
- the acquisition of businesses, products and technologies;
- our need to implement additional infrastructure and internal systems;
- our need to add personnel and financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company; and
- other risks and uncertainties, including those listed under Part I, Item 1A. "Risk Factors".

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I, Item 1A. "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

PART I

Item 1. Business.

Overview

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

We believe that our Synthetic Biotic platform has potential to address both metabolic and immune-mediated diseases and we are evaluating these medicines at different sites of action via different routes of administration, either orally or via injection. While we have designed and created a number of bacterial strains that could potentially be used therapeutically in a range of diseases, our initial focus is on metabolic diseases that could potentially be treated following oral delivery of a living medicine to the gut. This includes metabolic diseases, which include rare genetic diseases as well as metabolic diseases caused by organ dysfunction. When delivered orally, Synthetic Biotic medicines are designed to act from the gut to compensate for a dysfunctional metabolic pathway that results in the toxic accumulation of a metabolite with the intended consequence of reducing the systemic levels of the metabolite. We believe that success in our lead programs in rare metabolic diseases 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). SYNB1020, our first therapeutic program to enter clinical trials, is an oral therapy intended for the treatment of hyperammonemia, which includes patients with liver disease such as hepatic encephalopathy (HE) and patients with urea cycle disorders (UCD). In 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. SYNB1020 has received both Fast Track Designation and orphan drug designation for UCD from the U.S. Food and Drug Administration (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 March 2018, we initiated a clinical trial in patients with cirrhosis and elevated blood ammonia to evaluate the safety and tolerability of SYNB1020 as well as the ability of this Synthetic Biotic medicine to lower systemic levels of ammonia. We expect to have top-line data from this study in mid-2019. Upon receipt of satisfactory evidence of ammonia lowering in patients with cirrhosis, we will determine the clinical development path for SYNB1020 for the treatment of conditions resulting in hyperammonemia.

SYNB1618, our second program to enter clinical trials, is an oral therapy intended for the treatment of PKU, a rare metabolic disease 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 function in the gut of patients to reduce excess Phe, with the goal of lowering levels in the blood and other tissues. SYNB1618 has received both Fast Track designation and orphan drug designation for PKU from the FDA. We initiated a Phase 1 / 2a clinical trial for SYNB1618 in April 2018 and announced top-line data from this study in September 2018 that demonstrated that SYNB1618 was safe and well-tolerated and achieved proof-of-mechanism in healthy volunteers and we are currently evaluating SYNB1618 in patients with PKU. We expect to have patient data from this study in mid-2019.

We have developed a portfolio of immuno-oncology (IO) programs designed to deliver activities to modify the tumor microenvironment, activate the immune system and result in tumor reduction, and we envision that multiple engineered functions could be combined in one Synthetic Biotic medicine. These products could also be used in combination with other cancer therapies such as check-point inhibitors. In November 2018, we announced the selection of our first Synthetic Biotic clinical IO candidate, SYNB1891, and have advanced it into preclinical studies to enable filing of an Investigational New Drug (IND) application with the FDA in the second half of 2019. SYNB1891 is an intratumorally administered Synthetic Biotic medicine designed to act as a dual innate activator of the immune system by stimulation via the *E.coli* Nissle chassis and production of cyclic di-AMP, an activator of the STING pathway.

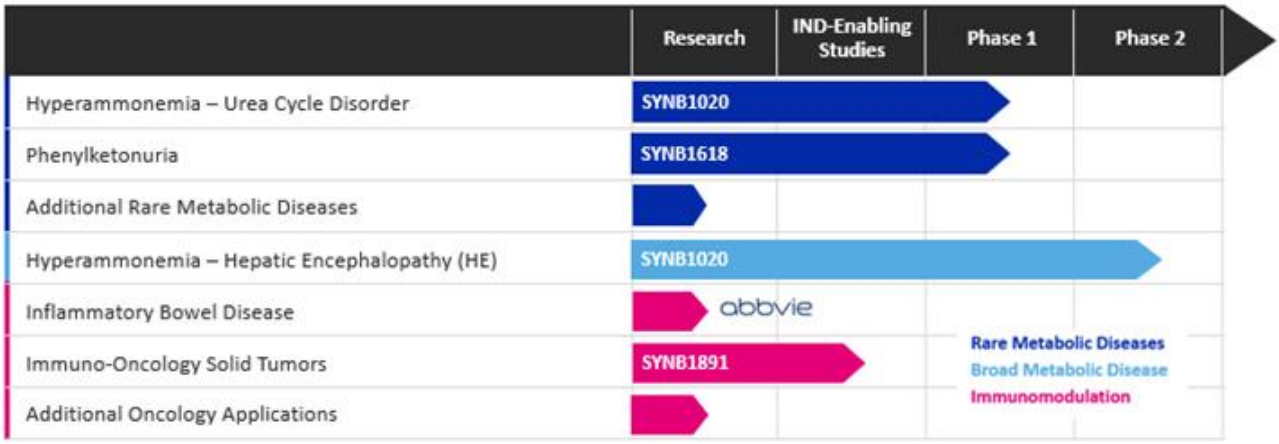
Our early-stage metabolic pipeline includes discovery-stage product candidates for rare metabolic diseases, GI and immune disorders with high unmet needs. We are also leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including metabolic diseases, inflammation and cancer. Synthetic Biotic medicines can be designed to locally deliver combinations of complementary therapeutics to treat these complex disease states.

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, manufacturing and commercialization, while also enhancing our industry-leading position in synthetic biology and metabolic engineering.

We 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. We have also established a technology collaboration with Ginkgo Bioworks, a privately held high-throughput synthetic biology company, to enable the discovery of new living medicines. We may enter into additional strategic partnerships in the future to maximize the value of our programs and our Synthetic Biotic platform.

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 laboratories of Professors James Collins and Timothy Lu from the Massachusetts Institute of Technology (MIT), who remain highly engaged in guiding development and application of our platform.

Our pipeline of our programs is shown below.



As we advance our lead programs, we continue to learn and improve 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:

Advance Clinical Development of the SYNB1020 Hyperammonemia Program. We initiated our first Phase 1 clinical trial of SYNB1020 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, achieved proof-of-mechanism and enabled us to identify a dose that could be taken forward into a study in patients. In April 2018, we initiated the first clinical trial of a Synthetic Biotic medicine in patients to evaluate SYNB1020 in individuals with cirrhosis as a result of liver disease who had elevated blood ammonia. We expect to have top-line data from this study by mid-2019. Further clinical development of SYNB1020 as a treatment for conditions resulting in hyperammonemia, including HE and UCDs, will be informed by a number of factors, including data from our Phase 1b / 2a study in patients with cirrhosis.

Advance Clinical Development of SYNB1618 for PKU. We initiated a Phase 1 / 2a clinical trial of SYNB1618 in April 2018. The Phase 1 / 2a clinical trial protocol included healthy volunteers, as well as adult patient cohorts, and is designed to assess safety, tolerability and pharmacodynamics. In September 2018, we announced top-line data from this study that demonstrated that SYNB1618 was safe in healthy volunteers, achieved proof-of-mechanism and enabled us to identify a dose for evaluation in patients with PKU. We expect to have data from the patient cohorts of this study, including insights regarding therapeutic potential from mechanistic biomarkers, by mid-2019. With supportive data from this study we expect to advance SYNB1618 to a larger clinical trial to assess its impact on blood Phe levels in patients with PKU.

Advance our first IO program into Clinical Development and Continue to Advance our Preclinical Pipeline. We are advancing IND-enabling studies of SYNB1891, our first IO program, with the goal of filing an IND application in the second half of 2019. We plan to continue to leverage our expertise from our lead programs to accelerate development of discovery-stage Synthetic Biotic programs in lead optimization for the potential treatment of rare metabolic, GI and immune disorders with high unmet needs.

Support Clinical Pipeline Progress with Expanded Manufacturing and Formulation Capability. In December 2018, we announced the expansion of our manufacturing capabilities to produce clinical trial material for mid-stage studies of our rare metabolic disease and IO programs, through entry into an agreement to lease good manufacturing practice (GMP) clean-room space in Waltham, Massachusetts. The new clean-room facility provides an affordable and flexible option that maximizes control over our processes and timelines enabling us to move efficiently through clinical development to bring our Synthetic Biotic medicines to patients.

Maximize the Value of the Synthetic Biotic Platform by Leveraging Strategic Partnerships. Our current partnership with AbbVie is focused on the discovery and development of Synthetic Biotic-based therapies for the treatment of IBD, and in November 2018 we announced receipt of a second milestone payment for this program. We expect to continue to explore strategic partnerships that would leverage the complementary capabilities of our partners to develop Synthetic Biotic medicines and maximize the value of our Synthetic Biotic platform.

Expand the Synthetic Biotic Platform to Lead in the Discovery and Development of Additional Living Medicines and Enabling Technologies. As leaders in the development of engineered non-pathogenic bacteria for therapeutic use, we intend to advance 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 intend 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 innovative product candidates that address a broad range of diseases. We have established a technology collaboration with Ginkgo Bioworks, a privately held high-throughput synthetic biology company, to enable the discovery of new living medicines.

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 non-pathogenic bacteria. We intend to continue to protect and leverage our intellectual property assets by maintenance and expansion of our worldwide portfolio of intellectual property, including the pursuit of composition of matter and other intellectual property focused on our Synthetic Biotic programs and our technology platform.

Our Focus: Living Medicines

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

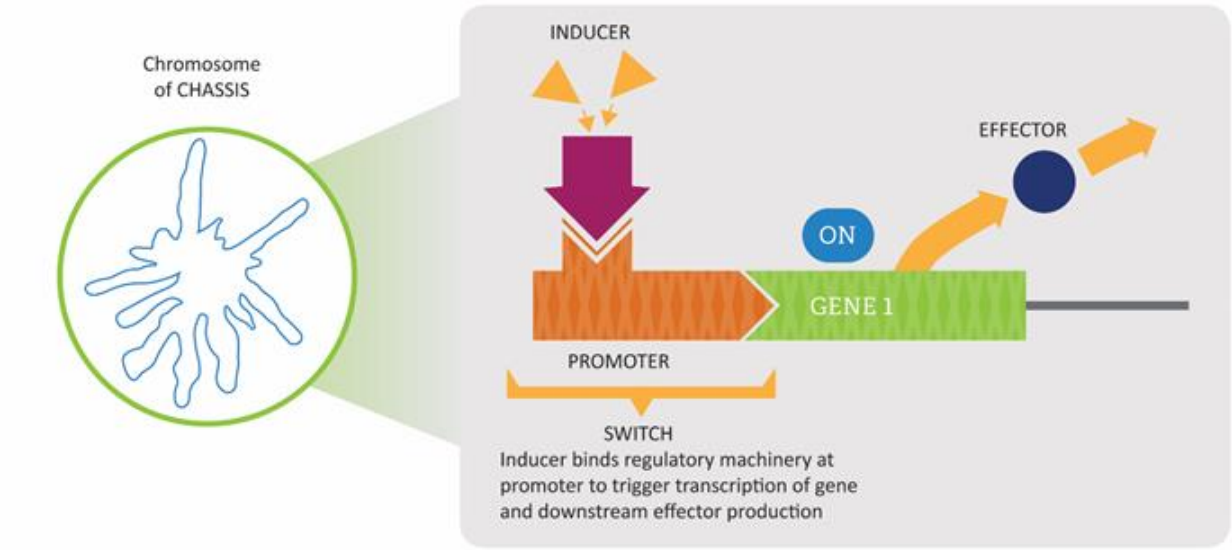
We believe living medicines have unique advantages as potential therapeutics. Living cells can carry out functions that cannot be performed by many conventional drug treatments, such as small molecules or antibodies. In contrast to conventional therapeutics that largely engage a single target and address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

Leveraging Synthetic Biology and Metabolic Engineering of Non-Pathogenic Bacteria to Produce Living Medicines

Non-Pathogenic Bacteria. Bacteria is isolated from the human microbiota and widely used as supplements that are believed to provide health benefits. Bacteria have evolved over millions of years to adapt, survive, and carry out active metabolism in many different environments. They are also amenable to genetic manipulation. To confer a therapeutic effect, we leverage basic biological properties of bacteria and tools of synthetic biology to develop Synthetic Biotic medicines.

Using Synthetic Biology to Generate Synthetic Biotic Medicines. Our scientists genetically engineer a beneficial non-pathogenic 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 non-pathogenic 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 potency, performance and output of the effectors themselves. We aim to precisely and appropriately control the amount, location and activity of our Synthetic Biotic medicines to address specific diseases.

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

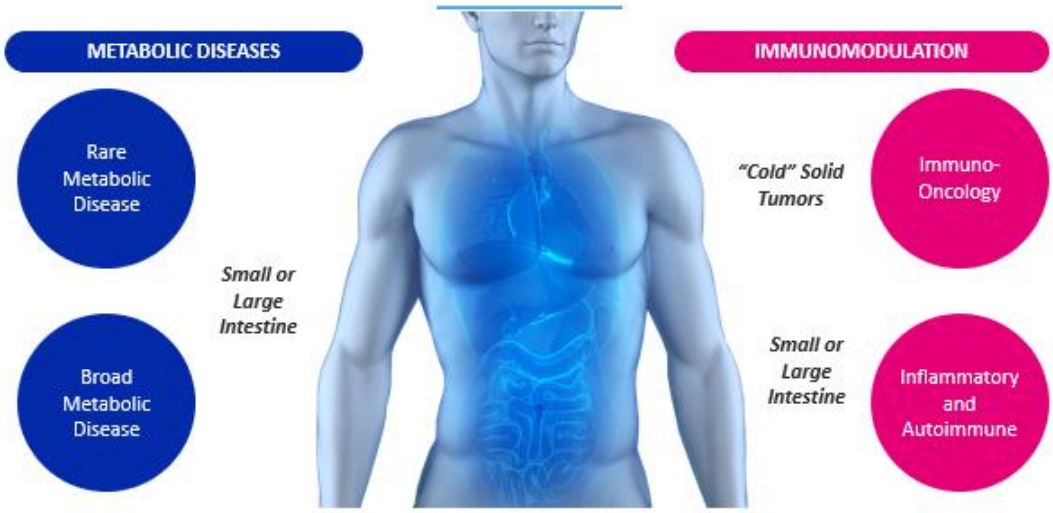


(1) The Chassis: Our Synthetic Biotic platform currently employs well-characterized bacteria used as probiotics to serve as the chassis upon which we build our living medicines. Our initial programs use *E. coli* Nissle, which is one of many non-pathogenic strains isolated from the human microbiota. *E. coli* Nissle is non-colonizing in the GI and has been used as a probiotic bacterial supplement for the last 20 years to promote gut health. Clinical studies have demonstrated that *E.coli* Nissle is 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 (*Sci. Transl. Med.* 2019: Vol. 11, Issue 475, eaau7975). 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 benefit. *E. coli* Nissle's metabolic systems and its genetic and metabolic machinery are well understood and provide a robust cellular context into which genetic information can be introduced with high efficiency and little or no damage to the fitness of the bacterium. In addition, the advanced nature of the synthetic biology toolkit available for *E. coli* Nissle enables rapid iterative design, assembly, and testing of prototype product candidates and remains unique among other bacterial and cellular engineering approaches.

(2) Building the Effector Module or Circuit: Synthetic Biotic medicines have the advantage that they can be designed with multiple pathway components. 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 and stable expression of multiple genes encoding enzymes and other proteins. 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. Our Synthetic Biotic platform allows us to engineer two types of mechanistic activities into our Synthetic Biotic medicines: we can engineer living medicines that act as engines capable of metabolic transformations that can substitute or compensate for missing or defective pathways in a patient, and we can also engineer living medicines to produce therapeutically beneficial molecules. We have leveraged proprietary tools, know-how and intellectual property to build multiple Synthetic Biotic lead strains that produce therapeutically relevant effects in preclinical 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 into our Synthetic Biotic medicines, with the goal of controlling the engineered circuit or its therapeutic output. To optimize the fitness of a Synthetic Biotic strain, it is critical that the effector is activated only at the appropriate time and place. The switches are based on engineering DNA elements called "inducible promoters" that are designed to sense and respond to disease states, specific environmental signals, or exogenously added inducing molecules. Our goal is to design and develop Synthetic Biotic medicines programmed with switches to produce therapeutic effects at precisely the right time and location such as the anaerobic environment of the gut, or in the context of local inflammation or other pathogenic factors.

Synthetic Biotic Portfolio: Initial Applications Designed to Target Different Sites of Action in Metabolic and Immune-mediated Diseases



Advantages of Our Synthetic Biotic Drug Development Platform and 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

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. We believe that our approach has advantages for the treatment of metabolic diseases, GI and immune disorders versus those other modalities that may be limited by delivery, transduction efficiency, duration of therapeutic expression and unclear potential for long-term dosing.

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.

Local Therapeutic Delivery: Production of One or More Effectors at the Site of Disease

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.

Our Synthetic Biotic programs for rare metabolic diseases are designed to be dosed orally, and act locally while transiting through the gut and, as a consequence, decrease toxic metabolite levels in the blood, thereby providing a systemic therapeutic benefit to the patient. 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 and the gut. Given the potential for chronic oral dosing, Synthetic Biotic medicines may have benefits in terms of dose prediction and reversibility of activity.

Currently, many complex diseases, such as inflammatory and autoimmune indications and cancer, require that patients are treated systemically with a combination of therapeutic agents, often resulting in poor tolerability, multiple adverse events and increased cost of therapy. Combinations of cytokine, antibody and protein therapies have potential for great benefit, but can be restricted by dose-limiting side effects when administered systemically. 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 toxic negative impact of multiple systemic therapies. We believe that 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 also developed approaches to enhance the secretion of protein effectors to the extracellular environment. We are developing Synthetic Biotic medicines with the potential to normalize function of a dysregulated immune system. 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 produce effectors to promote immune system activity against a tumor. These activities may further be combined with mechanisms that target tumor metabolism. 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.

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.

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 programs. 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, which limits patient-to-patient variability. 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 through 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 used for 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 where we have developed and executed processes to manufacture 3,000 to 5,000 doses of active drug. In December 2018, we entered into an agreement to lease GMP clean-room space from the Azzur Group, LLC. The agreement has expanded our manufacturing capabilities to enable in-house manufacturing of liquid and solid formulations for mid-stage clinical trials of our orally administered and IO Synthetic Biotic medicines.

Our Product Pipeline

Approach to Selection of Therapeutic Area

We believe that our Synthetic Biotic platform has potential to address both metabolic and immune-mediated diseases and we are evaluating these medicines at different sites of action via different routes of administration, either orally or via injection. Our approach to selecting our initial metabolic programs was 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 have been focused on certain rare metabolic diseases and acquired metabolic diseases that share these characteristics. When delivered orally, these 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 that clinical success in these programs 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 hyperammonemia (SYNB1020) and PKU (SYNB1618). Our early-stage metabolic pipeline includes discovery-stage product candidates for rare metabolic and GI tract diseases.

We are also leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including metabolic diseases, inflammation and cancer. We are developing a portfolio of IO programs capitalizing on the natural immunostimulatory characteristic of our bacterial chassis and using a rational approach to engineer specific effectors to stimulate the innate and adaptive arms of the immune system, alter the tumor microenvironment and to select combinations of relevant mechanisms and treatments to address specific tumor types.

Our Initial Programs: Overview of Rare Metabolic Diseases

Patients with rare metabolic diseases are born with mutations in certain 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 such diseases, 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, high unmet medical need remains as there are few current therapeutic treatments.

While there are hundreds of genetic conditions that fall into this class, individual disorders 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. This includes diseases such as urea cycle and amino acid metabolism disorders. Many rare metabolic diseases are thought to be underdiagnosed given the rarity of the conditions, potential for infant death and 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 nitrogen-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.

We believe that because the majority of ammonia is produced in the gastrointestinal (GI) tract, an orally administered Synthetic Biotic medicine could be an effective therapeutic to reduce the levels of excess ammonia in the blood of patients with HE and UCDs without the need for severe protein restriction and the risk of systemic toxicities. The FDA granted SYNB1020 orphan drug designation for UCDs in August 2016 and Fast Track designation in June 2017.

Overview of HE

The primary function of the liver is to filter out toxins, particularly ammonia, that are harmful if not correctly 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%.

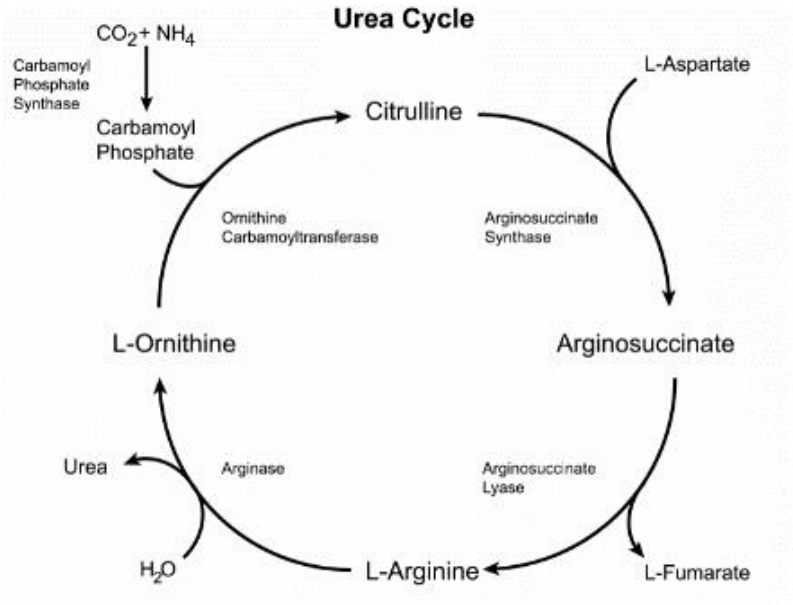
The current standard of care for overt HE includes lactulose, a non-absorbable disaccharide that prevents the absorption of ammonia in the gut. Lactulose is associated with GI side effects including both painful abdominal cramping and diarrhea. Non-absorbable antibiotics are also used to treat HE, often 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. There is a need for an effective therapy for patients with HE to reduce episodes of cognitive dysfunction and hospitalizations.

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



Urea Cycle: The urea cycle is a series of five enzymes as well as transporters and cofactors found primarily and the liver and intestine that are involved in the detoxification of ammonia. A sixth enzyme, N-acetylglutamate synthase (not shown) forms an important precursor for this pathway. Deficiencies in any of these six enzymes or damage to hepatocytes containing these enzymes can result in the toxic accumulation of ammonia or urea cycle intermediates.

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 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, although patients must 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, 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 concentrations at a safe level while allowing patients to eat a normal or only moderately restricted diet.

SYNB1020 Design

SYNB1020 is an orally administered, engineered strain of *E. coli* Nissle. SYNB1020 was designed to complement the missing or deficient enzyme functions in patients with hyperammonemia with an enhanced pathway to consume ammonia. This mechanism 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 as well as the potential to treat the spectrum of enzyme deficiencies that underlie UCD.

Our approach was to create a Synthetic Biotic medicine that would continuously consume excess ammonia where it is naturally produced in the colon 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.

A detailed description of the engineering of SYNB1020, data from preclinical studies in animal models of disease and healthy non-human primates as well as data from our clinical study of SYNB1020 in healthy volunteers was published in January 2019 (*Sci. Transl. Med.* 2019:Vol. 11, Issue 475, eaau7975).

In summary, we have demonstrated in *in vitro* studies, that SYNB1020 consumes ammonia and produces arginine at substantially higher rates compared with a control strain of *E. coli* Nissle that had not been engineered.

In an animal model of hyperammonemia, the *spf-ash*/F1 mouse, we observed a dose-dependent decrease in blood ammonia in mice fed a high protein diet that 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. Similar data demonstrating reduction in blood ammonia with SYNB1020 administration have been generated in both a mouse model (the thioacetamide, or TAA model) and in the rat bile duct ligation model of liver damage.

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 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 single ascending dose (SAD) portion of the study and 24 subjects in three cohorts of the multiple ascending dose (MAD) portion of the trial. Complete safety results from the SAD and MAD Phase 1 trials demonstrate that SYNB1020 was well tolerated at doses of up to $5x10^{11}$ CFU three times a day 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 blood ammonia levels. In a stable-isotope tracer study in which subjects were orally administered ^{15}N-ammonium chloride, we observed a dose-dependent increase in ^{15}Nitrate, a terminal metabolite of arginine metabolism, in plasma and urine compared to baseline in SYNB1020-treated subjects but not in the placebo group. In subjects treated with the highest dose, the increase in blood and urinary nitrate was statistically-significant compared to placebo-treated subjects. This observation is consistent with SYNB1020's mechanism of action which converts ammonia into arginine. In addition, conversion of ammonia into arginine was demonstrated in bacteria collected from the feces of treated subjects but not from placebo treated individuals thus demonstrating SYNB1020 retained activity during transit through the colon.

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 amounts of SYNB1020 detected in the feces increased with increasing SYNB1020 dose and that the bacteria behave in a consistent and predictable way with all subjects completely excreting and clearing SYNB1020 from their systems within two weeks after the final dose.

SYNB1020 Upcoming Milestones

In April 2018, we initiated the first clinical trial of SYNB1020 in patients with cirrhosis as a result of liver disease who had elevated blood ammonia and we expect to have top-line data by mid-2019. Further clinical development of SYNB1020 for conditions resulting in hyperammonemia, including HE and UCDs, will be informed by a number of factors, including data from our Phase 1b / 2a study in patients with cirrhosis.

SYNB1618 for PKU

PKU is a rare metabolic disease 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. There are currently two approved medications for treatment of PKU:

- Kuvan ® (sapropterin dihydrochloride), an oral medication that is indicated for a subgroup of patients who have some residual PAH activity and does not eliminate the need for ongoing dietary management.
- Palynziq™ (pegvaliase-pqpz), an injectable, pegylated, bacterial enzyme (phenylalanine ammonia-lyase or PAL) that metabolizes Phe and that is indicated for treatment of adult patients.

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 rare metabolic disease program, SYNB1618 for PKU, is designed to remove excess Phe from the blood by transforming it into non-toxic metabolites. The FDA granted SYNB1618 orphan drug designation for PKU in October 2017 and Fast Track designation in April 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, 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.

Palynziq™ (pegvaliase-pqpz), a pegylated form of recombinant phenylalanine ammonia lyase (PAL), an enzyme that metabolizes phenylalanine but does not require cofactor activity, was approved by the FDA in 2018. While daily Palynziq injections have been proven to lower phenylalanine levels, many patients experience injection site reactions and/or develop antibodies to the product. A Black Box warning of a risk of anaphylaxis is included on the Palynziq label and Palynziq is currently only indicated for adult patients. Other therapeutics in early development include various gene therapy approaches, modified cell therapies and a modified orally delivered enzyme replacement therapy.

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 consume 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 complementary pathways to reduce phenylalanine levels.

In designing SNYB1618, we integrated genes, including a form of the PAL enzyme that converts phenylalanine to the non-toxic byproduct *trans* cinnamic acid (TCA), which is then converted in the liver to hippurate (HA) and excreted in the urine. TCA and HA function as useful biomarkers of SYNB1618 activity *in vivo*. A detailed description of the engineering of SYNB1618 and data from preclinical studies in an animal model of disease and healthy non-human primates was published in September 2018 (Nat. Biotechnol. 36, 857–864 (2018)).

SYNB1618 Nonclinical Program

Preclinical Efficacy Studies

In vivo studies in a mouse model of PKU *(enu2-/-)* demonstrated that urinary HA concentrations increased in a dose-dependent fashion in SYNB1618-treated mice compared to mice treated with an unengineered *E. coli* Nissle control that did not have the phenylalanine degradation pathway. We also observed that subcutaneous injection of mice on a Phe-restricted diet with phenylalanine resulted in a rapid increase in blood phenylalanine concentrations. The increase associated with this phenylalanine challenge was significantly blunted upon oral administration of SYNB1618 compared to administration of the non-engineered control strain. Similar data were generated with SYNB1618 in healthy non-human primates. With increasing oral doses of SYNB1618, we observed increasing levels of plasma TCA and urinary HA demonstrating that SYNB1618 is functional in the primate gut.Taken together, these data demonstrate that SYNB1618 has activity in the GI tract and can decrease blood Phe levels by degradation of recirculating phenylalanine, as well as dietary Phe. A detailed description of the engineering of SYNB1618 and data from preclinical studies in an animal model of disease and healthy non-human primates was published in September 2018 (Nat. Biotechnol. 36, 857–864 (2018)).

SYNB1618 Clinical Development Plan

In April 2018, we initiated a Phase 1 / 2a, randomized, double-blinded, placebo-controlled study to evaluate the safety, tolerability, and gastrointestinal clearance of SYNB1618. We treated healthy adult volunteers with single- or multiple-ascending doses of SYNB1618 and are currently evaluating SYNB1618 in cohorts of patients with PKU.

Primary endpoints of the study were safety, tolerability and identification of a suitable dose to evaluate in patients with PKU. In addition, exploratory endpoints were designed to evaluate the pharmacodynamic effects of SYNB1618, including production of previously identified biomarkers related to SYNB1618 activity, TCA in plasma and HA in urine, and to provide mechanistic and clinical insights in both healthy volunteers and patients with PKU.

Fifty-six healthy volunteers were dosed orally with either SYNB1618 or placebo (ratio three to one), including 24 in six cohorts in the SAD portion of the study and 32 subjects in three cohorts of the MAD portion of the trial. In September 2017, we announced top-line data demonstrating that in healthy volunteers SYNB1618 was safe and well tolerated at doses up to $2x10^{11}$ CFU three times a day for seven days. Higher doses were associated with mild to moderate gastrointestinal symptoms, mainly nausea and vomiting. The data also demonstrated proof-of-mechanism for SYNB1618.

During the treatment part of the study, subjects were housed in a clinical unit and provided a defined diet. The activity of SYNB1618 was evaluated in fasted subjects in both the SAD and MAD cohorts after administration of a standardized breakfast drink containing a defined amount of protein. At one dose level in the SAD portion of the study, solid food containing an equivalent amount of protein was substituted for the liquid meal. In addition, a labeled Phe tracer (D5-Phe) was orally administered. Blood and urine were collected over a subsequent six-hour period and several metabolites were measured including Phe and SYNB1618-specific biomarkers of Phe metabolism, TCA in blood and HA in urine. This was conducted in the SAD cohorts on the day of dosing and in the MAD cohorts on Day -1 (baseline) and Day 7 (the last day of dosing).

A statistically significant dose-dependent increase in both plasma TCA and urinary HA was observed in SYNB1618-treated subjects but not in those treated with placebo. Production of metabolites from Phe administered as a free amino acid was similar to Phe administered as whole protein. In addition, production of metabolites was similar whether the protein was administered as a liquid or as a solid meal. In healthy volunteers, who all have normal Phe metabolism, there was no impact on blood Phe levels. All healthy volunteers enrolled in the study cleared SYNB1618 from their GI tracts within the expected timeframe

SYNB1618 Upcoming Milestones

The Phase 1/2a trial is ongoing and we are currently evaluating single and multiple doses of SYNB1618 in patients with PKU. The primary endpoints of the study are safety and tolerability. In addition, while the study was not designed to demonstrate and effect on Phe lowering it will enable evaluation of the pharmacodynamic effects of SYNB1618, including production of TCA in plasma and HA in urine in order to characterize the kinetics of SYNB1618 and to provide mechanistic and clinical insights in patients with PKU. We expect to have data in mid-2019.

Synthetic Biotic Medicines for Rare Metabolic, GI and Immune Disorders with High Unmet Needs

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 rare metabolic diseases 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 rare metabolic, GI and immune disorders with high unmet needs.

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 of the liver and central nervous system. For these indications, there is need for a safe, oral therapies with local activity in the gut to reset a metabolic dysfunction.

Synthetic Biotic Medicines for Immunomodulation

Our Synthetic Biotic platform has the potential to generate clinically meaningful therapies for patients affected by immune-mediated diseases.

Our Synthetic Biotic Medicines for Immuno-Oncology (IO)

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, have responded 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 current immunotherapy.

Our goal is to leverage our Synthetic Biotic platform to design living medicines that can engage multiple immunomodulatory pathways to enhance tumor inflammation and promote robust T cell responses enabling broad tumor response and remission. We believe that such medicines have the potential to expand the patient population that could benefit from immunotherapy. Our approach is designed to deliver robust therapeutic combinations directly 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 (consumption of an immune-suppressive metabolite or production of an immuno-activating metabolite, secretions or bacterial surface display of proteins (cytokines, chemokines, receptor ligands), and secretion or bacterial surface display of specific single chain antibody domains, known as scFv.

We believe our Synthetic Biotic platform can be deployed 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, our first Synthetic Biotic development program is SYNB1891, an engineered E.coli Nissle designed to produce a STING (STimulator of INterferon Genes) agonist while taking advantage of the chassis effect. The STING pathway plays a critical role in the control of tumor growth at both steady state and following a variety of cytolytic and immune-based therapies by initiating an antitumor immune response and driving tumor regression. SYNB1891 can be delivered directly into the tumor enabling its localized site of action in the tumor microenvironment. The approach of using intra-tumoral injection elicits STING activation in the tumor but not systematically, potentially decreasing the risk of adverse events that may arise from the production of systemic interferon.
- *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 kynurenine to reprogram the tumor microenvironment and to enable recognition of the tumor by the adaptive immune system.

- *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 and scFvs 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 the immune augmentation and T cell expansion effects of kynurenine consumption. In early studies with intra-tumoral administration, in preclinical mouse models, we have observed high rates of durable response with evidence of an effect not only on the treated tumor, but also a shrinking of tumors outside the scope of the localized treatment (abscopal effect), while avoiding systemic toxicity.

In 2018, we selected SYNB1891 as our first Synthetic Biotic IO development candidate and are advancing it through IND-enabling studies. We expect to file an IND application for SYNB1891 in the second half of 2019.

Our Synthetic Biotic Medicines for Inflammatory Bowel Disease

Among immune conditions, IBD is particularly attractive for our Synthetic Biotic platform, 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 Synthetic Biotic medicines for the treatment of IBD. In June 2017 and September 2018, we announced the achievement of the first and second milestones, respectively in this collaboration.

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 a key role in 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.

Collaboration Agreements

To accelerate the development and commercialization of Synthetic Biotic medicines to patients, 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 an 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 milestones.

In May 2017, IBDCo achieved the first of these research milestones under the AbbVie Agreements for which it received $2.0 million. On September 27, 2018, AbbVie and the Company signed an amendment (the Second Amendment) to the AbbVie Agreements. The Second Amendment clarified the requirements necessary to complete the second phase which resulted in additional time and effort in the second phase of the research plan. Additionally, the Second Amendment split the next milestone payment under the AbbVie Agreements into two payments: a milestone payment of $2.0 million earned by the Company upon execution of the Second Amendment and the remaining milestone payment of the balance due upon the successful achievement of specified research and pre-clinical events and the advancement to the third phase of the research plan.

On December 18, 2018, AbbVie and the Company signed an amendment (the Third Amendment) to the AbbVie Agreements. The Third Amendment provides that in the event AbbVie determines that it is necessary to enter into license agreements with certain third parties in a particular country or other jurisdiction which, but for such license, would be infringed by the manufacture, use or sale of any product governed by the AbbVie Agreements, AbbVie would be entitled to deduct certain expenses related to such license agreements from particular payments made to the Company.

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 and Technology Licenses

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 certain 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 metabolic disorders, autoimmune and other inflammatory disorders and oncology. As of March 5, 2019, we had 106 Synlogic-owned patents and patent applications in U.S. and foreign jurisdictions, of which 5 have been issued or allowed.

Synlogic Intellectual Property

Disease-related applications

The disease-related applications in our intellectual property portfolio relate to certain pathological conditions including, but not limited to hyperammonemia, hyperphenylalaninemia, diseases and conditions arising from IEMs, metabolic disorders diseases and conditions associated with an inflammatory state, diseases associated with gut inflammation, compromised gut mucosal barrier (leaky gut), and various autoimmune disorders as well as use in immuno-oncology and provide coverage for engineered bacteria having genetic circuitry designed to specifically address those conditions and the associated disease states. The intellectual property portfolio provides coverage for compositions directed to engineered bacterial strains, methods of making the bacterial strains and methods for treating diseases. Currently, intellectual property relating to this technology includes pending applications in U.S. and foreign jurisdictions, as well as several issued U.S. patents directed to composition of matter and pharmaceutical composition claims covering our clinical candidates. The patent term for our current IP has expiration dates ranging from December 2035 to February 2037, depending on the indication and 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.

Technology Licenses

In addition to our own patent applications, we have historically licensed patents and patent applications from MIT and Trustees of Boston University (BU) to access intellectual property covering synthetic biology circuitry. The intellectual property licensed from MIT and BU related 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.

During 2018, we determined our growing portfolio of internally generated intellectual property superseded the in-licensed intellectual property in the BU license and the MIT license. Accordingly, on December 18, 2018, we provided notice to terminate the license agreements with MIT and BU/MIT. The BU license will be terminated effective February 16, 2019 and the MIT license will be terminated effective June 19, 2019.

General Considerations

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 (USPTO) 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”.

Trademarks

Our registered trademark portfolio currently contains 14 registered trademarks, and eight pending applications

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”.

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 IND application 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 GMP 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 biotherapeutic products. This Guidance reflects the FDA's thinking on a topic at the time that it was issued and although it 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 the 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.

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 GMP 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 reactions, 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 a significant user fee; although a waiver of such fee may be obtained under certain limited circumstances, including where the biologic has been designated as an orphan drug. 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. The 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 are 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 approval 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 newly approved 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 the 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 USPTO, 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 BLA.

Pediatric exclusivity is a type of marketing exclusivity available in the United States. Under the Best Pharmaceuticals for Children Act (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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, 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 orphan drug designation for SYNB1020 for the treatment of UCDs. In October 2017, the FDA granted SYNB1618 orphan drug designation for the treatment of PKU.

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 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.

In June 2017, the FDA granted Fast-Track designation for the use of SYNB1020 for the treatment of UCDs.

In April 2018, the FDA granted Fast-Track designation for the use of SYNB1618 for the treatment of PKU.

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 GMP 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. The 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 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 prices 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 us to reproducibly manufacture high quality living medicines at clinical scale and, later, at commercial scale to enable approval of our product candidates. We have an internal development group and have recently expanded our manufacturing and process development capabilities with the lease of GMP cleanroom space in Waltham, Massachusetts. This facility enables us to produce clinical trial material for early to mid-stage studies of our rare metabolic disease and IO programs. We continue to build the organization to support scale-up and development towards commercialization. We currently expect to continue to work with contract manufacturing organizations (CMOs) for production of late-stage clinical trial material.

Clinical trial material for our Phase 1 studies of SYNB1020 for hyperammonemia and SYNB1618 for PKU were manufactured by a CMO. These first clinical trials used a liquid formulation. We have invested in the development of a solid dose oral formulation for later stage clinical development and commercial use.

To enable the production of high levels of cells, or biomass, 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 increase our scale and eventually 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 will compare the merits of working with one or more CMOs who meet our criteria with the possibility of building GMP 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 non-pathogenic bacteria, our clinical development expertise, and strong 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 an approved product; and
  - Acer Therapeutics Inc., Aeglea Biotherapeutics, Inc. and Ultragenyx Pharmaceutical Inc., have products in clinical testing. Kaleido Biosciences, Inc. is evaluating a product in a non-IND study. Arcturus Therapeutics Inc., Selecta Biosciences, Inc., Translate Bio, Inc. and Versantis AG each have discovery or pre-clinical stage product candidates in development.
- *HE*
  - Bausch Health Companies has an approved product; and
  - Mallinckrodt plc, Rebiotix, Inc./Ferring and Umecrine Cognition AB have programs in clinical testing. Kaleido Biosciences, Inc. is evaluating a product in a non-IND study. Several other pre-clinical and discovery stage companies are developing product candidates.

- *PKU*
  - BioMarin, Inc. has two approved products and a development stage product; and
  - Censa Pharmaceuticals, Inc. and Codexis, Inc. have products in clinical trials. Rubius Therapeutics, Inc., Homology Medicines, Inc., Moderna Inc., Agios Pharmaceuticals, Inc. and others are developing product candidates.
- *IO*
  - The field of immuno-oncology is highly competitive with many companies developing and commercializing a wide range of types of pharmaceutical products and combinations. Companies with STING agonists in clinical development include Aduro BioTech, Inc., in partnership with Novartis AG, Merck & Co. Inc. and GlaxoSmithKline plc. Examples of companies developing other modalities include companies such as Merck and Bristol-Myers Squibb Company that develop and market antibodies called checkpoint inhibitors. Celgene Corporation (currently undergoing a merger with Bristol-Myers Squibb) and Gilead Sciences, Inc. market autologous cell-based therapies called CAR-T. Other companies are developing and or marketing oncolytic viruses, cancer vaccines, cytotoxic agents, and other approaches to treating cancer.

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; Paul Miller, Ph.D., 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 March 5, 2019, we had 74 full-time employees. Of our full-time employees, 58 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.

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 (Exchange Ratio). In addition, 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 the Exchange Ratio multiplied by the number of shares of Private Synlogic common stock previously represented by such options. Mirna also assumed the 2017 Plan.

Our Internet address is www.synlogictx.com. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Securities and Exchange Commission (SEC).

Item 1A. 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. Furthermore, these factors represent risks and uncertainties that could cause actual results to differ materially from those implied by forward-looking statements. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Quarterly Report on Form 10-Q and our other public filings with the SEC. The following risk factors may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

In the following discussion of risk factors, References to "we", "us", "our" and similar terms refer to the combined business of Synlogic, Inc. after the Merger on August 28, 2017.

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 Biotic medicines and we have incurred significant operating losses since our inception. Our net loss was approximately $48.4 million and $40.4 million for the fiscal years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of approximately $119.8 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 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. 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 the Merger. 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 in healthy volunteers, in April 2018, we announced that we dosed the first patient in our Phase 1b / 2a clinical trial of SYNB1020 for treatment of hyperammonemia in patients with cirrhosis, and in April 2018 we dosed our first subject in a Phase 1 / 2a clinical trial of SYNB1618 which is being developed for the treatment of patients with PKU, 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. 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 identifying or reaching agreement on acceptable terms with third-party manufacturers, delays in developing and transferring a reproducible, scalable manufacturing process, 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 and/or clinical trials, 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 Biotic medicines 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 medicines 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. 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 diseases 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 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 has 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, none of our product candidates has advanced into any pivotal clinical trial, for our proposed indications and it may be years before any pivotal clinical trials 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 may be 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 costs might be higher than expected and 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 pre-existing 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 and for SYNB1618 in April 2018. 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 (GMP) 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 GMP and adherence to commitments made in any 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.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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 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.

We may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base, and thereby decrease our revenue.

In many activities, including the conduct of clinical trials, we are subject to laws and regulations governing data privacy and the protection of health-related and other personal information. These laws and regulations govern our processing of personal data, including the collection, access, use, analysis, modification, storage, transfer, security breach notification, destruction and disposal of personal data. We must comply with laws and regulations associated with the international transfer of personal data based on the location in which the personal data originates and the location in which it is processed. Although there are legal mechanisms to facilitate the transfer of personal data from the European Economic Area (EEA), and Switzerland to the United States, the decision of the European Court of Justice that invalidated the safe harbor framework has increased uncertainty around compliance with EU privacy law requirements. As a result of the decision, it was no longer possible to rely on safe harbor certification as a legal basis for the transfer of personal data from the European Union to entities in the United States. In February 2016, the European Commission announced an agreement with the Department of Commerce, or DOC, to replace the invalidated safe harbor framework with a new EU-U.S. "Privacy Shield." On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the European Court of Justice in its recent ruling by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and Federal Trade Commission and making commitments on the part of public authorities regarding access to information.

The privacy and security of personally identifiable information stored, maintained, received or transmitted, including electronically, is subject to significant regulation in the United States and abroad. While we strive to comply with all applicable privacy and security laws and regulations, legal standards for privacy continue to evolve and any failure or perceived failure to comply may result in proceedings or actions against us by government entities or others, or could cause reputational harm, which could have a material adverse effect on our business.

Numerous foreign, federal and state laws and regulations govern collection, dissemination, use and confidentiality of personally identifiable health information, including state privacy and confidentiality laws (including state laws requiring disclosure of breaches); federal and state consumer protection and employment laws; HIPAA; and European and other foreign data protection laws. These laws and regulations are increasing in complexity and number, may change frequently and sometimes conflict.

HIPAA establishes a set of national privacy and security standards for the protection of individually identifiable health information, including protected health information, or PHI, by health plans, certain healthcare clearinghouses and healthcare providers that submit certain covered transactions electronically, or covered entities, and their ''business associates,'' which are persons or entities that perform certain services for, or on behalf of, a covered entity that involve creating, receiving, maintaining or transmitting PHI. While we are not currently a covered entity or business associate under HIPAA, we may receive identifiable information from these entities. Failure to receive this information properly could subject us to HIPAA's criminal penalties, which may include fines up to $250,000 per violation and/or imprisonment. In addition, responding to government investigations regarding alleged violations of these and other laws and regulations, even if ultimately concluded with no findings of violations or no penalties imposed, can consume company resources and impact our business and, if public, harm our reputation.

In addition, various states, such as California and Massachusetts, have implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. California's patient privacy laws, for example, provide for penalties of up to $250,000 and permit injured parties to sue for damages. The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and our clients and potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify.

In addition, the interpretation and application of consumer, health-related, and data protection laws are often uncertain, contradictory, and in flux.

U.S.-based companies may certify compliance with the privacy principles of the Privacy Shield. Certification to the Privacy Shield, however, is not mandatory. If a U.S.-based company does not certify compliance with the Privacy Shield, it may rely on other authorized mechanisms to transfer personal data.

The privacy and data security landscape is still in flux. In October 2016, an action for annulment of the European Commission decision on the adequacy of Privacy Shield was brought before the European Court of Justice by three French digital rights advocacy groups, La Quadrature du Net, French Data Network and the Fédération FDN. This case, Case T738/16, is currently pending before the European Court of Justice. Should the European Court of Justice invalidate the Privacy Shield, it will no longer be possible to transfer data from the European Union to entities in the United States under a Privacy Shield certification, in which case other legal mechanisms would need to be put in place.

The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects our business.

In the United States, California recently adopted the California Consumer Privacy Act of 2018, or CCPA, which will come into effect beginning in January 2020. The CCPA has been characterized as the first "GDPR-like" privacy statute to be enacted in the United States because it mirrors a number of the key provisions of the EU General Data Protection Regulation. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches.

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. 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 medicines, 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 Biotic medicines. 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 and expect to enter into additional license agreements in the future. Our existing agreements impose, and future license agreements may 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 make 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 development 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 late-stage 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 to manufacture late-stage 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.

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.

Synthetic Biotic medicines are complex and difficult to manufacture. We could experience production or technology transfer problems that result in delays in our development or commercialization schedules or otherwise adversely affect our business. Issues with the manufacturing process, even minor deviations from the normal process, could result in insufficient yield, product deficiencies or manufacturing failures that result in lot failures, insufficient inventory, and product recalls.

Many factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god beyond our control. We also may encounter problems in hiring and retaining the experienced specialized personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing processes or facilities could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs, result in delays in our clinical development or marketing schedules and harm our business.

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 GMP regulations. Any of our suppliers or manufacturers could fail 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 could become limited or interrupted for other reasons. Under these circumstances, we may choose or be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, manufacture in collaboration with a third-party at their facilities, 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, which may impact our potential economic benefits;
- 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.

Risks Related to Commercialization of Our Product Candidates

If any of our product candidates is 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, Acer Therapeutics, Inc., Aeglea BioTherapeutics, Inc., Arcturus Therapeutics Inc., Ultragenyx Pharmaceutical Inc., Horizon Pharma plc, Kaleido Biosciences, Inc., Selecta Biosciences, Inc., Translate Bio, Inc. and Versantis AG have developed or are developing product candidates for the treatment of UCD; Bausch Health Companies Inc., Kaleido Biosciences, Inc., Mallinckrodt plc, Rebiotix, Inc./Ferring, Umecrine Cognition AB, Versantis AG as well as other preclinical and discovery stage companies have developed or are each developing product candidates for the treatment of HE; and American Gene Technologies International Inc., BioMarin, Inc., Censa Pharmaceuticals, Inc., Codexis, Inc., Homology Medicines, Inc., MipSalus ApS, Moderna Therapeutics, and Rubius Therapeutics, 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, chief executive officer, and chief medical officer, chief financial 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 Our Common Stock

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 March 5, 2019, our executive officers and directors, together with holders of 5% or more of our common stock outstanding and their respective affiliates, beneficially own approximately 55.9% 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 March 5, 2019 there were a total of 25,400,495 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 executive officers are parties to employment agreements providing for aggregate cash payments of up to approximately $1.5 million at December 31, 2018 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters and operations are located in Cambridge, Massachusetts. We currently lease 41,346 square feet of laboratory and office space at 301 Binney Street and until February 2018, we leased 14,390 square feet of laboratory and office space at 200 Sidney Street, both in Cambridge, Massachusetts. The agreement to terminate the lease for the 200 Sidney Street space occurred in July 2017 in conjunction with the execution of the lease for the space in the 301 Binney Street facility. Our 301 Binney Street lease expires in 2028. We believe that our facilities are suitable and adequate for our needs for the foreseeable future.

Item 3. Legal Proceedings.

From time to time, we are subject to various legal proceedings, claims and administrative proceedings that arise in the ordinary course of our business activities. Although the results of the litigation and claims cannot be predicated with certainty, as of the date of this report, we do not believe we are party to any claim, proceeding or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock has been traded on The Nasdaq Capital Market under the symbol "SYBX" since August 28, 2017, prior to which it was traded under the symbol "MIRN".

Stockholders

As of March 5, 2019, there were approximately 215 stockholders of record of our common stock.

Dividends

We have never declared or paid any dividends to our stockholders since our inception and we do not plan to declare or pay cash dividends in the foreseeable future. We currently anticipate that we will retain any future earnings for the operation and expansion of our business.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Forward-Looking Information

The Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K, the audited financial statements and accompanying notes, included elsewhere in this Annual Report on Form 10-K, and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read together. In addition to historical information, this discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Operating results are not necessarily indicative of results that may occur for the full fiscal year or any other future period. The term "Private Synlogic" refers to Synlogic, Inc. prior to the consummation of the Merger described herein. The term "Mirna" refers to Mirna Therapeutics, Inc. prior to the consummation of the Merger described herein. Unless otherwise indicated, references to the terms "Synlogic," "the Company," "we," "our" and "us" refer to Private Synlogic prior to the consummation of the Merger described herein and Synlogic, Inc. (formerly known as Mirna Therapeutics, Inc.) upon the consummation of the Merger described herein.

Overview

Recent Developments

Recent Offerings of Synlogic Common Stock

In January 2018, we sold 5,899,500 shares of our common stock through a firm commitment, underwritten public offering at a price to the public of $9.75 per share. As a result of the offering, including the exercise of the overallotment option, we received aggregate net proceeds, after underwriting discounts and commissions and other estimated offering expenses, of approximately $53.8 million.

In April 2018, we sold 3,280,000 shares of our common stock at a price of $9.15 per share in a registered direct offering. After fees and other offering expenses, we received approximately $28.9 million in net proceeds from the offering.

Merger with Mirna

In August 2017, Synlogic, Inc., formerly known as Mirna Therapeutics, Inc. (NASDAQ: MIRN) (Mirna), completed its business combination with Synlogic, Inc. (Private Synlogic when referred to prior to the Merger) 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). As part of the Merger, Mirna was renamed Synlogic, Inc. (Public Synlogic) and Private Synlogic was renamed Synlogic Operating Company, Inc. Following completion of the Merger, Private Synlogic, now known as Synlogic Operating Company, Inc., is the surviving corporation of the Merger and a wholly-owned subsidiary of Public Synlogic. The Merger has been accounted for as a "reverse merger" under the acquisition method of accounting for business combinations with Private Synlogic treated as the accounting acquirer of Mirna. The historical financial statements of Private Synlogic have become the historical financial statements of Public Synlogic, or the combined company, and are included in this Annual Report on Form 10K filing labeled Synlogic, Inc. As a result of the Merger, historical common stock, preferred stock, stock options and additional paid-in capital, including share and per share amounts, were retroactively adjusted to reflect the equity structure of Public Synlogic, including the effect of the Merger exchange ratio and the Public Synlogic common stock par value of $0.001 per share. See "*Merger with Mirna Therapeutics*" within Note 3 of the notes to our audited consolidated financial statements for the year ended December 31, 2018 included in this Annual Report on Form 10-K for additional discussion of the Merger and the exchange ratio.

Pursuant to the terms of the Merger Agreement and after giving effect to a reverse stock split, at the effective time of the Merger (the Effective Time), each outstanding share of Private Synlogic capital stock was converted into the right to receive approximately 0.5532 shares of Mirna common stock (the Exchange Ratio). In addition, at the Effective Time, Mirna assumed all outstanding options to purchase shares of Private Synlogic common stock, which were exchanged for options to purchase shares of Mirna common stock, in each case appropriately adjusted based on the Exchange Ratio. Mirna also assumed the Synlogic 2017 Stock Incentive Plan (the 2017 Plan).

Business

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

We believe that our Synthetic Biotic platform has potential to address both metabolic and immune-mediated diseases and we are evaluating these medicines at different sites of action via different routes of administration, either orally or via injection. While we have designed and created a number of bacterial strains that could potentially be used therapeutically in a range of diseases, our initial focus is on metabolic diseases that could potentially be treated following oral delivery of a living medicine to the gut. This includes metabolic diseases, which include rare genetic diseases as well as metabolic diseases caused by organ dysfunction. When delivered orally, Synthetic Biotic medicines are designed to act from the gut to compensate for a dysfunctional metabolic pathway that results in the toxic accumulation of a metabolite with the intended consequence of reducing the systemic levels of the metabolite. We believe that success in our lead programs in rare metabolic diseases 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). SYNB1020, our first therapeutic program to enter clinical trials, is an oral therapy intended for the treatment of hyperammonemia, which includes patients with liver disease such as hepatic encephalopathy (HE) and patients with urea cycle disorders (UCD). In 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. SYNB1020 has received both Fast Track Designation and orphan drug designation for UCD from the U.S. Food and Drug Administration (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 March 2018, we initiated a clinical trial in patients with cirrhosis and elevated blood ammonia to evaluate the safety and tolerability of SYNB1020 as well as the ability of this Synthetic Biotic medicine to lower systemic levels of ammonia. We expect to have top-line data from this study in mid-2019. Upon receipt of satisfactory evidence of ammonia lowering in patients with cirrhosis, we will determine the clinical development path for SYNB1020 for the treatment of conditions resulting in hyperammonemia.

SYNB1618, our second program to enter clinical trials, is an oral therapy intended for the treatment of PKU, a rare metabolic disease 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 function in the gut of patients to reduce excess Phe, with the goal of lowering levels in the blood and other tissues. SYNB1618 has received both Fast Track designation and orphan drug designation for PKU from the FDA. We initiated a Phase 1 / 2a clinical trial for SYNB1618 in April 2018 and announced top-line data from this study in September 2018 that demonstrated that SYNB1618 was safe and well-tolerated and achieved proof-of-mechanism in healthy volunteers and we are currently evaluating SYNB1618 in patients with PKU. We expect to have patient data from this study in mid-2019.

We have developed a portfolio of immuno-oncology (IO) programs designed to deliver activities to modify the tumor microenvironment, activate the immune system and result in tumor reduction, and we envision that multiple engineered functions could be combined in one Synthetic Biotic medicine. These products could also be used in combination with other cancer therapies such as check-point inhibitors. In November 2018, we announced the selection of our first Synthetic Biotic clinical IO candidate, SYNB1891, and have advanced it into preclinical studies to enable filing of an Investigational New Drug (IND) application with the FDA in the second half of 2019. SYNB1891 is an intratumorally administered Synthetic Biotic medicine designed to act as a dual innate activator of the immune system by stimulation via the *E.coli* Nissle chassis and production of cyclic di-AMP, an activator of the STING pathway.

Our early-stage metabolic pipeline includes discovery-stage product candidates for rare metabolic diseases, GI and immune disorders with high unmet needs. We are also leveraging our proprietary technology platform to develop Synthetic Biotic medicines to treat a broader range of human diseases, including metabolic diseases, inflammation and cancer. Synthetic Biotic medicines can be designed to locally deliver combinations of complementary therapeutics to treat these complex disease states.

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, manufacturing and commercialization, while also enhancing our industry-leading position in synthetic biology and metabolic engineering.

We 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. We have also established a technology collaboration with Ginkgo Bioworks, a privately held high-throughput synthetic biology company, to enable the discovery of new living medicines. We may enter into additional strategic partnerships in the future to maximize the value of our programs and our Synthetic Biotic platform.

We currently operate in one reportable business segment—the discovery and development of Synthetic Biotic medicines. To date, we have dedicated substantially all of our activities to the research and development of our product candidates. As of March 2019, we have received approximately $240.4 million in proceeds to date as we financed our operations through approximately $110.7 million in aggregate net proceeds from the sale of Private Synlogic preferred stock and Synlogic, LLC preferred units, approximately $0.4 million in a convertible promissory note with one of our investors, which was converted into Private Synlogic preferred stock, approximately $6.0 million in payments received under the AbbVie Agreement, approximately $40.4 million from our merger with Mirna, net of transaction costs, approximately $82.7 million in total net proceeds from the sale of our common stock in our common stock offerings in January and April 2018 and $0.2 million from exercises of stock options.

We have not generated any revenue to date from product sales and have incurred significant operating losses since our inception. We have incurred net losses of approximately $48.4 million and $40.4 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018 and 2017, we had an accumulated deficit of approximately $119.8 million and $71.7 million, respectively, and we expect to incur losses for the foreseeable future as we develop our product candidates. We expect our expenses and capital requirements will increase substantially in connection with our ongoing activities, as we:

- complete preclinical studies, initiate and complete clinical trials for product candidates;
- contract to manufacture product candidates;
- advance research and development related activities to expand our product pipeline;
- seek regulatory approval for our product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, and management personnel;
- expand our existing infrastructure and secure space in a facility to support continued growth in our research and development efforts; and
- add operational and finance personnel to support product development efforts and to support operating as a public company.

We do not expect to generate product revenue unless and until we successfully complete clinical development and obtain regulatory approvals for our product candidates, either alone or in collaboration with third parties. Additionally, we expect to utilize third-party contract research organizations (CROs) and contract manufacturing organizations (CMOs) to carry out our clinical development and manufacturing activities, and we do not yet have a commercial organization. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution. Accordingly, we anticipate that we will seek to fund our operations through public or private equity or debt financings, collaborations or licenses, capital lease transactions or other available financing transactions. However, we may be unable to raise additional funds through these or other means when needed. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if it will be able to achieve or maintain profitability. Even if we are able to generate product revenue, we may not become profitable.

Financial Overview

Revenue

Revenue to date is generated from our collaboration agreement with AbbVie. The collaboration agreement contains multiple deliverables, which include an exclusive option for AbbVie to acquire IBDCo and research and development milestones. See Note 14, "Significant Agreements" in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a full discussion of this arrangement. We expect our revenue to fluctuate for the foreseeable future as it is principally based on the achievement of research and development milestones under our collaboration agreement with AbbVie.

Research and Development Expense

Research and development expense consists of expenses incurred in connection with the discovery and development of our product candidates, including the conduct of preclinical and clinical studies and product development, which are expensed as they are incurred. These expenses consist primarily of:

- compensation, benefits and other employee related expenses;
- supplies to support our internal research and development efforts;
- research and development related facility and depreciation costs; and
- third-party contract costs relating to research, process and formulation development, preclinical and clinical studies and regulatory operations.

The lengthy process of securing regulatory approvals for new drugs requires the expenditure of substantial resources. Any delay or failure to obtain regulatory approvals would materially adversely affect our product candidate development efforts and our business overall. Given the inherent uncertainties of pharmaceutical product development, we cannot estimate with any degree of certainty the likelihood, timing or cost of obtaining regulatory approval and marketing our product candidates and thus, when, if ever, our product candidates will generate revenues and cash flows.

The successful development of our product candidates is highly uncertain and subject to a number of risks. Refer to the risk factors under the heading *Risks Related to the Development of Our Product Candidates* in Part II, Item 1A, found elsewhere in this Annual Report on Form 10-K.

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical data of each product candidate, as well as the competitive landscape and ongoing assessments of such product candidate's commercial potential. We expect our research and development costs will be substantial for the foreseeable future. We expect costs associated with our SYNB1020 and SYNB1618 programs to increase as the programs progress through and into clinical trials.

We track direct research and development expenses, consisting principally of external costs, such as costs associated with contract research organizations and manufacturing of preclinical and clinical drug product and other outsourced research and development expenses to specific product programs. Costs related to specific product candidates are tracked upon the selection of a product candidate. We do not allocate employee and consulting-related costs, costs associated with our platform and facility expenses, including depreciation or other indirect costs, to specific product candidate programs because these costs are deployed across multiple product candidate programs under research and development and, as such, are separately classified. The table below summarizes our research and development expenses by categories of costs for the periods presented (in thousands):

	Year ended December 31,	
	2018	2017
SYNB1020	$ 2,924	$ 5,528
SYNB1618	6,245	3,564
External pre-development candidate expenses and unallocated expenses	5,728	8,615
Internal research and development expenses	23,137	12,634
	$ 38,034	$ 30,341

General and Administrative Expense

General and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, investor relations, business development and human resource functions. Other costs include the legal costs of pursuing patent protection of our intellectual property, general and administrative related facility and information technology infrastructure costs and professional fees for accounting and legal services. We anticipate increases in expenses related to operating as a public company. These increases include legal fees, accounting fees, costs for director and officer liability insurance, fees for investor relations services and costs associated with implementing and complying with corporate governance, internal controls and similar requirements applicable to public companies. We charge all general and administrative expenses to operations as incurred.

Other Income (Expense)

Interest and investment income consists primarily of income earned on investments. Interest expense consists of expense related to our capital leases. Other expense consists primarily of gains and losses on foreign currency invoices.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the U.S.(GAAP). The preparation of these financial statements requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, the reported amounts of revenues and expenses during the reported periods and related disclosures. These estimates and assumptions, including those related to revenue recognition and research and development expenses are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. These critical estimates and assumptions are based on our historical experience, our observance of trends in the industry, and various other factors that are believed to be reasonable under the circumstances and form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from our estimates under different assumptions or conditions.

We believe that the application of the following accounting policies, each of which require significant judgments and estimates on the part of management, are the most critical to aid in fully understanding and evaluating our reported financial results. Our significant accounting policies are more fully described in Note 2, “Summary of Significant Accounting Policies”, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Revenue Recognition

Effective January 1, 2018, we adopted Accounting Standards Codification (ASC) Topic 606, *Revenue from Contracts with Customers* (ASC 606) using the modified retrospective transition method. See Note 2 “Summary of Significant Accounting Policies”, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. Under this method, results for reporting periods beginning on and after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC Topic 605, *Revenue Recognition* (ASC 605).

We evaluate collaboration agreements with respect to FASB ASC Topic 808, *Collaborative Arrangements*, considering the nature and contractual terms of the arrangement and the nature of our business operations to determine the classification of the transactions. When we are an active participant in the activity and exposed to significant risks and rewards dependent on the commercial success of the collaboration, we will record our transactions on a gross basis in the consolidated financial statements and describe the rights and obligations under the collaborative arrangement in the notes to the consolidated financial statements.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five-step analysis: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step analysis to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We may enter into collaboration agreements for research and development services, under which we may license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, upfront license fees; reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Variable consideration is constrained until it is deemed not be at significant risk of reversal.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements for which the collaboration partner is also a customer, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the contract term and pattern of satisfaction of the performance obligations under step (v) above. We use significant judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to the goods and services we expect to provide. We use estimates to determine the timing of satisfaction of performance obligations, which may include the use of full time equivalent time as a measure of satisfaction of performance obligations.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Licenses of Intellectual Property

In assessing whether a promise or performance obligation is distinct from the other promises, we consider factors such as the research, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. In addition, we consider whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and Development Services

If an arrangement is determined to contain a promise or obligation for us to perform research and development services, we must determine whether these services are distinct from the other promises in the arrangement. In assessing whether the services are distinct from the other promises, we consider the capabilities of the customer to perform these same services. In addition, we consider whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For research and development services that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer Options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. We evaluate the customer options for material rights, that is, the option to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on an alternative approach when the goods or services are both (i) similar to the original goods and services in the contract and (ii) provided in accordance with the terms of the original contract. Under this alternative, we allocate the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to a material right are not recognized as revenue until the option is exercised and the performance obligation is satisfied.

Milestone Payments

At the inception of each arrangement that includes milestone payments, we evaluate whether a significant reversal of cumulative revenue provided in conjunction with achieving the milestones is probable and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, we evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

Contract Costs

We recognize as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. As a practical expedient, we recognize the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that we otherwise would have recognized is one year or less. To date, we have not incurred any incremental costs of obtaining a contract with a customer.

Research and Development Expense

All research and development expenses are expensed as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including compensation, benefits and other employee costs; equity-based compensation expense; laboratory and clinical supplies and other direct expenses; facilities expenses; overhead expenses; fees for contractual services, including preclinical studies, clinical trials, clinical manufacturing and raw materials; and other external expenses. Nonrefundable advance payments for research and development activities are capitalized and expensed over the related service period or as goods are received. When third-party service providers' billing terms do not coincide with our period-end, we are required to make estimates of our obligations to those third parties, including clinical trial costs, contractual service costs and costs for supply of our drug candidates, incurred in a given accounting period and record accruals at the end of the period. We base our estimates on our knowledge of the research and development programs, services performed for the period and the expected duration of the third-party service contract, where applicable.

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial results.

	Year ended December 31,	
	2018	2017
	(in thousands)	
Revenue	$ 2,520	$ 2,444
Operating expenses:		
Research and development	38,034	30,341
General and administrative	15,716	12,927
Total operating expenses	53,750	43,268
Loss from operations	(51,230)	(40,824)
Other income (expense):		
Interest and investment income	2,843	504
Interest expense	(43)	(57)
Other expense	(5)	—
Other income (expense), net	2,795	447
Net loss	$ (48,435)	$ (40,377)

Year Ended December 31, 2018 Compared to Year Ended December 31, 2017

Revenue

	Years Ended December 31,		Change	
	2018	2017	$	%
	(dollars in thousands)			
Revenue	$ 2,520	$ 2,444	$ 76	3%

Revenue was $2.5 million for the year ended December 31, 2018 compared to $2.4 million for the year ended December 31, 2017. Revenue for the years ended December 31, 2018 and 2017 was related to the recognition of deferred revenue from services performed and payments received under the AbbVie collaboration.

Operating Expenses

	Years Ended December 31,		Change	
	2018	2017	$	%
	(dollars in thousands)			
Operating expenses:				
Research and development	$ 38,034	$ 30,341	$ 7,693	25%
General and administrative	15,716	$ 12,927	2,789	22%
Total operating expenses	$ 53,750	$ 43,268	$ 10,482	24%

Research and Development Expense

Research and development expense was $38.0 million for the year ended December 31, 2018 compared to $30.3 million for the year ended December 31, 2017. The increase of $7.7 million was primarily due to an increase of $3.2 million in clinical development costs associated with our SYNB1618 program, primarily due to our Phase 1 / 2a clinical trial, $4.7 million in compensation, benefits and other employee-related expenses associated with increased headcount and equity-based compensation, $1.2 million in expenses associated with external preclinical studies and $3.7 million of research and development support costs. Research and development support costs include increased rent and depreciation from our 301 Binney Street facility in Cambridge, Massachusetts which we occupied in January 2018. These increases were partially offset by decreases of $1.8 million in equity-based charges and $0.3 million in patent related charges both associated with the MIT-BU license signed in April 2017, as well as a decrease of $1.6 million in manufacturing and formulation costs associated with our SYNB1020 and SYNB1618 programs and a decrease of $1.4 million in clinical development costs primarily related to our SYNB1020 program.

General and Administrative Expense

General and administrative expense was $15.7 million for the year ended December 31, 2018 compared to $12.9 million for the year ended December 31, 2017. The increase of $2.8 million was due primarily to an increase of $4.1 million in compensation, benefits and other employee-related expenses associated with increased headcount and equity-based compensation, inclusive of $1.7 million equity-based compensation charges and $0.8 million of severance payments primarily related to the departure of our former Chief Executive Officer, as well as an increase of $0.5 million related to insurance and taxes and $0.1 million in corporate fees related to our investments in marketable securities and public company activities, including filing fees. The increases were partially offset by a decrease of $1.1 million in legal fees associated with both corporate and patent legal expenses and a decrease in audit fees of $0.8 million.

Other Income (Expense)

	Years Ended December 31,		Change	
	2018	2017	$	%
	(dollars in thousands)			
Other income (expense):				
Interest and investment income	$ 2,843	$ 504	$ 2,339	464%
Interest expense	(43)	(57)	14	(25)%
Other expense	(5)	—	(5)	N/A
Other income (expense), net	$ 2,795	$ 447	$ 2,348	525%

Other income (expense) for the year ended December 31, 2018 was $2.8 million compared to $0.5 million for the corresponding period in 2017. The increase of $2.3 million was related to an increase in interest and investment income resulting from higher cash balances and higher interest rates generated by our investment account. Additionally, interest expense decreased during the year as the capital leases established during 2017 were paid down. The net increase was partially offset by an increase in other expense associated with foreign currency invoices.

Liquidity and Capital Resources

We have incurred losses since our inception on March 14, 2014 and, as of December 31, 2018, we had an accumulated deficit of approximately $119.8 million. We have financed our operations to date primarily through the sale of preferred stock, common stock, preferred units, payments received under our AbbVie collaboration agreement, interest earned on investments, and cash received in the Merger. At December 31, 2018, we had approximately $122.7 million in cash, cash equivalents, and marketable securities. Our cash and cash equivalents include amounts held in money market funds and corporate debt securities, stated at cost plus accrued interest, which approximates fair market value. Our available-for-sale securities include amounts held in corporate debt securities. We invest cash in excess of immediate requirements in accordance with our investment policy, which limits the amounts we may invest in any one type of investment and requires all investments held by us to maintain minimum ratings from Nationally Recognized Statistical Rating Organizations so as to primarily achieve liquidity and capital preservation.

During the year ended December 31, 2018 our cash, cash equivalents and marketable securities balance increased approximately $35.7 million. The increase was primarily due to the net proceeds of $53.8 million from the sale of our common stock through a firm commitment, underwritten public offering in January 2018 and $28.9 million in net proceeds from the registered direct sale of our common shares in April 2018. These increases were partially offset by the cash used to operate our business, including payments related to, among other things, research and development and general and administrative expenses as we continue to invest in our primary drug candidates and support the development of our proprietary platform. We also made capital purchases and made payments on our capital leases, net of transaction costs, received in the Merger. The increase was partially offset by the cash used to operate our business, including payments related to, among other things, research and development and general and administrative expenses as we continued to invest in our primary drug candidates and support the development of our proprietary platform.

The following table sets forth the major sources and uses of cash for each of the periods below:

	Years ended December 31,	
	2018	2017
	(in thousands)	
Net cash, cash equivalents and restricted cash (used in) provided by		
Operating activities	$ (42,470)	$ (31,055)
Investing activities	(87,201)	9,278
Financing activities	82,483	66,678
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (47,188)	$ 44,901

Cash Flows from Operating Activities

Net cash, cash equivalents and restricted cash used in operating activities totaled approximately $42.5 million for the year ended December 31, 2018. The primary use of cash was our net loss of approximately $48.4 million and an increase in working capital of $0.6 million, primarily related to decreases in accounts payable and accrued expenses and deferred revenue offset by an increase in deferred rent from our 301 Binney Street facility. Net loss was partially offset by $5.3 million of non-cash items primarily including depreciation and equity-based compensation.

Net cash, cash equivalents and restricted cash used in operating activities totaled approximately $31.1 million for the year ended December 31, 2017. The primary use of cash was our net loss of approximately $40.4 million. These uses of cash were partially offset by non-cash items of approximately $6.7 million including equity-based compensation, depreciation and equity-based costs associated with the execution of a license agreement and approximately $2.6 million in working capital, primarily from increases in accounts payable and accrued expenses and decreases in deferred rent associated with the acceleration of recognition due to the 200 Sidney Street lease termination.

Cash Flows from Investing Activities

Net cash, cash equivalents and restricted cash used in investing activities for the year ended December 31, 2018 totaled approximately $87.2 million and resulted primarily from the purchases of securities of $172.9 million and the purchases of property and equipment of $5.7 million. These uses were partially offset by proceeds from the maturity of marketable securities of $91.3 million.

Net cash, cash equivalents and restricted cash provided by investing activities for the year ended December 31, 2017 totaled approximately $9.3 million and resulted from the $40.4 million in net proceeds received in the Merger and the proceeds from the maturity of marketable securities of $22.9 million. These proceeds were partially offset by uses of cash including the purchase of securities of $51.4 million and purchases of property and equipment of $2.6 million, including deposits related to the construction of leasehold improvements associated with the new facilities lease.

Cash Flows from Financing Activities

Net cash, cash equivalents and restricted cash provided by financing activities for the year ended December 31, 2018 totaled approximately $82.5 million and resulted primarily from $53.8 million in net proceeds from the sale of our common stock through a firm commitment, underwritten public offering in January 2018, $28.9 million in net proceeds from the sale of our common stock in April 2018 and proceeds from exercises of stock options of $0.2 million, partially offset by $0.4 million in payments on our capital leases.

Net cash, cash equivalents and restricted cash provided by financing activities for the year ended December 31, 2017 totaled approximately $66.7 million and resulted primarily from the net proceeds from the sale of Class B preferred units in March 2017 of $26.6 million and $40.4 million in net proceeds from the sale of Series C preferred stock in May 2017. These sources of cash were partially offset by $0.4 million of payments on our capital leases.

Funding Requirements

To date, we have not commercialized any products and have not achieved profitability. We anticipate that we will continue to incur substantial net losses for the next several years as we further develop our product candidates, invest in our proprietary platform technology and operate as a publicly traded company.

We have generated revenue from our AbbVie collaboration, but have not generated any product revenue since our inception and do not expect to generate any product revenue unless we receive regulatory approval for our product candidates. We believe that our cash on hand as of December 31, 2018 will be sufficient to meet our anticipated cash requirements for at least the next 12 months from the date of this filing. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially and negatively as a result of a number of factors, including the factors discussed in the section entitled "Risk Factors" in this Annual Report on Form 10-K. We have based our estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Due to the numerous risks and uncertainties associated with the development of our product candidates, we are unable to estimate precisely the amounts of capital outlays and operating expenditures necessary to complete the development of, and to obtain regulatory approval for, our product candidates. Our funding requirements will depend on many factors, including, but not limited to, the following:

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

As an early-stage company, we are subject to a number of risks common to other life science companies, including, but not limited to, the ability to raise additional capital, development by our competitors of new technological innovations, risk of failure in preclinical studies, the safety and efficacy of our product candidates in clinical trials, the regulatory approval process, the ability to efficiently manufacture our products, market acceptance of our products once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. Our therapeutic programs are currently pre-commercial, spanning discovery through early development and will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. There can be no assurance that our research and development will be successfully completed, that adequate protection for our intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if our product development efforts are successful, it is uncertain when, if ever, we will generate revenue from product sales. We may never achieve profitability, and unless and until we do, we will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or partnerships. If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Commitments and Obligations

Our commitments for operating leases relate to our lease of office and laboratory space at 301 Binney Street in Cambridge, Massachusetts.

In July 2017, we entered into an agreement to lease approximately 41,346 square feet of laboratory and office space at 301 Binney Street in Cambridge, Massachusetts. Annual rent is approximately $3.1 million. The ten-year lease commenced in January 2018 and contains provisions for a free-rent period, annual rent increases and an allowance for tenant improvements. Additionally, we have paid for 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.

On December 7, 2018, Synlogic Operating Company, Inc., a wholly-owned subsidiary of Synlogic, Inc. (the "Company"), entered into a Statement of Work (the "SOW") with Azzur Group, LLC ("Azzur") pursuant to a Master Contract Services Agreement (the "Master Services Agreement"), dated September 8, 2018, between the Company and Azzur.

Pursuant to the SOW, Azzur has agreed to provide the Company with access to, and the use of, an approximately 700 square foot cleanroom space to be constructed in Waltham, Massachusetts (the "Azzur Suite"), for a period of 44 months, from May 1, 2019 to December 31, 2022 (the "Term"). Azzur has also agreed to provide the Company with storage space and personnel support at the Azzur Suite. The total estimated project cost during the Term for access to, and use of, the cleanroom and storage space, and the personnel support and other services, is $4.8 million.

The Company may terminate the SOW on four months' prior written notice at any time during the Term. In addition, either party may terminate the Master Services Agreement (including the SOW) due to a breach by the other party and failure to cure. If the Azzur Suite is not ready for use by the Company as of May 1, 2019, the Company may (i) elect to terminate the SOW, (ii) wait for the Azzur Suite to become available, without incurring any costs (other than a deposit) relating to the Azzur Suite until it becomes available, or (iii) accept an alternate cleanroom space from Azzur on different terms.

As we are a clinical stage company, having entered the clinic for our first Phase 1 clinical trial in June 2017, we expect our most significant clinical trial expenditures will be with CROs and CMOs. These contracts generally are cancellable, with notice, at our option and do not have cancellation penalties.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, that would have been established for the purpose of facilitating off-balance sheet arrangements (as that term is defined in Item 303 (a)(4)(ii) of Regulation S-K) or other contractually narrow or limited purposes. As such, we are not exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in those types of relationships. We enter into guarantees in the ordinary course of business related to the guarantee of our performance and the performance of our subsidiaries.

JOBS Act

Section 107 of the JOBS Act 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. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other companies.

Recent Accounting Pronouncements

Please read Note 2, "Summary of Significant Accounting Policies" to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide this information required under this item.

Item 8. Consolidated Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the independent registered public accounting firm report thereon, appear at pages F-1 through F-37, respectively, of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Definition and limitations of disclosure controls

Our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act) are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed under the Exchange Act, such as this report, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures are also designed to ensure that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management evaluates these controls and procedures on an ongoing basis.

There are inherent limitations to the effectiveness of any system of disclosure controls and procedures. These limitations include the possibility of human error, the circumvention or overriding of the controls and procedures and reasonable resource constraints. In addition, because we have designed our system of controls based on certain assumptions, which we believe are reasonable, about the likelihood of future events, our system of controls may not achieve its desired purpose under all possible future conditions. Accordingly, our disclosure controls and procedures provide reasonable assurance, but not absolute assurance, of achieving their objectives.

Evaluation of Disclosure Controls and Procedures

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Changes in Internal Control

Other than discussed below, there have not been any changes in our internal controls over financial reporting identified in connection with the evaluation of such internal control that occurred during our fiscal quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as amended. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework. Based on our assessment, management believes that, as of December 31, 2018, our internal control over financial reporting is effective based on those criteria.

Inherent Limitations on the Effectiveness of Controls

A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the controls are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues or misstatements, if any, within a company have been detected. Accordingly, our controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our control system are met. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance Matters," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Conduct and Ethics" in the Company's Proxy Statement for the 2019 Annual Meeting of Stockholders.

Item 11. Executive Compensation.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Executive Officer and Director Compensation" in the Company's Proxy Statement for the 2019 Annual Meeting of Stockholders.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Security Ownership of Certain Beneficial Owners and Management" in the Company's Proxy Statement for the 2019 Annual Meeting of Stockholders.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Person Transactions" and "Management and Corporate Governance" in the Company's Proxy Statement for the 2019 Annual Meeting of Stockholders.

Item 14. Principal Accounting Fees and Services.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Independent Registered Public Accounting Firm" in the Company's Proxy Statement for the 2019 Annual Meeting of Stockholders.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

Item 15(a). The following documents are filed as part of this Annual Report on Form 10-K:

Item 15(a)(1) and (2) See "Consolidated Financial Statements and Supplementary Data" at Item 8 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable, or the information is included in the financial statements or notes thereto.

Item 15(a)(3) The following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
2.1^	Agreement and Plan of Merger and Reorganization, dated as of May 15, 2017, by and among Mirna Therapeutics, Inc., Meerkat Merger Sub, Inc. and Synlogic, Inc.		8-K (Exhibit 2.1)	5/16/2017	001-37566
3.1	Amended and Restated Certificate of Incorporation		8-K (Exhibit 3.1)	10/6/2015	001-37566
3.2	Certificate of Amendment (Reverse Stock Split) to the Amended and Restated Certificate of Incorporation, dated August 25, 2017		8-K (Exhibit 3.1)	8/28/2017	001-37566
3.3	Certificate of Amendment (Name Change) to the Amended and Restated Certificate of Incorporation		8-K (Exhibit 3.2)	8/28/2017	001-37566
3.4	Amended and Restated Bylaws		8-K (Exhibit 3.2)	10/6/2015	001-37566
4.1	Form of Common Stock Certificate		S-1/A (Exhibit 4.2)	9/18/2015	333-206544
10.1#	2015 Equity Incentive Award Plan		10-K (Exhibit 10.1)	3/20/2018	001-37566
10.2#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2015 Equity Incentive Award Plan.		S-1/A (Exhibit 10.9(B))	9/11/2015	333-206544
10.3#	Form of Restricted Stock Award Agreement and Restricted Stock Unit Award Grant Notice under the 2015 Equity Incentive Award Plan.		S-1/A (Exhibit 10.9(C))	9/11/2015	333-206544
10.4#	2017 Stock Incentive Plan		10-K (Exhibit 10.4)	3/20/2018	001-37566
10.5#	Form of Stock Option Grant Notice and Stock Option Agreement under 2017 Stock Incentive Plan.		10-Q (Exhibit 10.17)	11/13/2017	00-37566
10.6#	Non-Employee Director Compensation Program.		10-K (Exhibit 10.6)	3/20/2018	001-37566
10.7#	Form of Indemnification Agreement between the Company and each of its directors and officers		S-1/A (Exhibit 10.13)	9/11/2015	333-206544
10.8#	Offer Letter by and between Synlogic and Jose Carlos Gutierrez-Ramos, Ph.D., dated as of March 20, 2015		8-K (Exhibit 10.2)	8/28/2017	001-37566

10.9#	First Amendment to Offer Letter by and between Synlogic and Jose Carlos Gutierrez-Ramos, Ph.D., dated as of May 8, 2017		8-K (Exhibit 10.3)	8/28/2017	001-37566
10.10#	Letter Agreement dated as of May 9, 2018, between Synlogic, Inc. and Jose-Carlos Gutiérrez-Ramos		10-Q (Exhibit 10.2)	5/15/2018	001-37566
10.11#	Amendment to Option Agreements dated as of June 5, 2018, between Synlogic, Inc. and Jose-Carlos Gutiérrez-Ramos		10-Q (Exhibit 10.2)	8/9/2018	001-37566
10.12#	Offer Letter by and between Synlogic and Todd Shegog, dated as of June 17, 2016		8-K (Exhibit 10.4)	8/28/2017	001-37566
10.13#	First Amendment to Offer Letter by and between Synlogic and Todd Shegog, dated as of May 8, 2017		8-K (Exhibit 10.5)	8/28/2017	001-37566
10.14#	Offer Letter by and between Synlogic and Aoife M. Brennan, MB, BCh, BAO, MMSc, dated as of June 22, 2016		8-K (Exhibit 10.6)	8/28/2017	001-37566
10.15#	First Amendment to Offer Letter by and between Synlogic and Aoife M. Brennan, MB, BCh, BAO, MMSc, dated as of November 7, 2016		8-K (Exhibit 10.7)	8/28/2017	001-37566
10.16#	Second Amendment to Offer Letter by and between Synlogic and Aoife M. Brennan, MB, BCh, BAO, MMSc, dated as of May 8, 2017		8-K (Exhibit 10.8)	8/28/2017	001-37566
10.17#	Third Amendment to Offer Letter dated as of June 5, 2018, between Synlogic, Inc. and Aoife Brennan, MB, BCh, BAO, MMSc		10-Q (Exhibit 10.1)	8/9/2018	001-37566
10.18#	Amended and Restated Letter Agreement by and between Synlogic, Inc. and Aoife M. Brennan, MB, BCh, BAO, MMSc, dated as of October 1, 2018		10-Q (Exhibit 10.1)	11/13/2018	001-37566
10.19#	Amended and Restated Letter Agreement by and between Paul Miller, Ph.D., dated as of May 16, 2017		8-K (Exhibit 10.9)	8/28/2017	001-37566
10.20#	Employment Agreement, dated as of September 4, 2017, by and between the Company and Andrew W. Gengos.		8-K (Exhibit 10.1)	10/10/2017	001-37566
10.21#	Separation Agreement by and between the Company and Paul Lammers, dated as of August 20, 2017.		8-K (Exhibit 10.10)	8/28/2017	001-37566
10.22#	Separation Agreement by and between the Company and Alan Fuhrman, dated as of August 20, 2017.		8-K (Exhibit 10.11)	8/28/2017	001-37566
10.23†^	Agreement and Plan of Merger by and among AbbVie S.à.r.l., Suffolk Merger Sub, Inc., Synlogic IBDCo, Inc., Synlogic, LLC, Synlogic, Inc. and the founders named therein, dated as of July 16, 2015; as amended by a First Amendment to Agreement and Plan of Merger, dated as of December 14, 2015		8-K (Exhibit 10.12)	8/28/2017	001-37566
10.24†^	Second Amendment to Agreement and Plan of Merger by and among AbbVie S.à.r.l., Synlogic IBDCo, Inc. and Synlogic Operating Company, Inc., dated as of September 27, 2018		10-Q (Exhibit 10.2)	11/13/2018	001-37566
10.25†^	Third Amendment to Agreement and Plan of Merger and First Amendment to License Agreement by and among AbbVie S.à.r.l., Synlogic IBDCo, Inc. and Synlogic Operating Company, Inc., dated as of December 18, 2018	X			

10.26†	License Agreement by and between Synlogic, Inc. and Synlogic IBDCo, Inc., dated as of July 16, 2015		8-K (Exhibit 10.13)	8/28/2017	001-37566
10.27	Sales Agreement, dated as of October 13, 2017 by and between the registrant and Cowen and Company, LLC		8-K (Exhibit 1.1)	10/16/2017	001-37566
10.28	Form of Subscription Agreement, dated as of April 6, 2018, by and among Synlogic, Inc. and certain investors.		8-K (Exhibit 10.1)	4/6/2018	001-37566
10.29†	Master Contract Services Agreement, dated as of September 8, 2018, between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC).	X			
10.30†	Statement of Work dated September 10, 2018 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC).	X			
10.31†	Statement of Work dated December 7, 2018 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC).	X			
21.1	Subsidiaries of the registrant	X			
23.1	Consent of Independent Registered Accounting Firm	X			
24.1	Power of Attorney (included in the signature page hereto)	X			
31.1	Certification of Chief Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a).	X			
31.2	Certification of Chief Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a).	X			
32.1	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350).	X			
32.2	Certification required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350).	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

^ The schedules and exhibits to this exhibit have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

Management contract or compensatory plans or arrangements.

† Confidential treatment has been requested or granted as to certain portions, which portions have been omitted and filed separately with the SEC.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Synlogic, Inc.

Date: March 12, 2019

By: /s/ Aoife Brennan
Aoife Brennan
President, Chief Executive Officer and Chief Medical Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Aoife Brennan and Todd Shegog his true and lawful attorney-in-fact and agent, with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his name.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the registrant in the capacities indicated below and on the dates indicated.

Name	Title	Date
/s/ Aoife Brennan **Aoife Brennan**	President, Chief Executive Officer, Chief Medical Officer and Director *(Principal Executive Officer)*	March 12, 2019
/s/ Todd Shegog **Todd Shegog**	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 12, 2019
/s/ Peter Barrett **Peter Barrett**	Chairman of the Board	March 12, 2019
/s/ Patricia hurter **Patricia Hurter**	Director	March 12, 2019
/s/ Chau Khuong **Chau Khuong**	Director	March 12, 2019
/s/ Nick Leschly **Nick Leschly**	Director	March 12, 2019
/s/ Edward Mathers **Edward Mathers**	Director	March 12, 2019
/s/ Michael Powell **Michael Powell**	Director	March 12, 2019
/s/ Richard P. Shea **Richard P. Shea**	Director	March 12, 2019

Index to Consolidated Financial Statements of Synlogic, Inc.

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Synlogic, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Synlogic, Inc. and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, contingently redeemable preferred equity and stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2015.

Cambridge, Massachusetts
March 12, 2019

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Balance Sheets

(In thousands, except share amounts)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 11,252	$ 58,440
Short-term marketable securities	111,477	28,585
Prepaid expenses and other current assets	1,609	1,564
Total current assets	124,338	88,589
Property and equipment, net	14,841	9,783
Restricted cash	1,097	1,097
Other assets	64	230
Total assets	$ 140,340	$ 99,699
Liabilities, Contingently Redeemable Preferred Equity and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,380	$ 2,679
Accrued expenses	5,034	4,823
Deferred revenue	268	444
Deferred rent	393	656
Capital lease obligations	266	425
Total current liabilities	8,341	9,027
Long-term liabilities:		
Deferred revenue, net of current portion	—	668
Deferred rent, net of current portion	7,691	4,500
Capital lease obligations, net of current portion	210	466
Total long-term liabilities	7,901	5,634
Commitments and contingencies (Note 18)		
Stockholders' Equity		
Preferred stock, $0.001 par value		
5,000,000 shares authorized, none issued and outstanding as of December 31, 2018 and December 31, 2017	—	—
Common stock, $0.001 par value		
250,000,000 shares authorized as of December 31, 2018 and December 31, 2017. 25,401,479 shares issued and outstanding as of December 31, 2018 and 16,272,617 shares issued and outstanding as of December 31, 2017.	25	16
Additional paid-in capital	243,903	156,685
Accumulated other comprehensive loss	(65)	(9)
Accumulated deficit	(119,765)	(71,654)
Total stockholders' equity	124,098	85,038
Total liabilities and stockholders' equity	$ 140,340	$ 99,699

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Years ended December 31,	
	2018	2017
Revenue	$ 2,520	$ 2,444
Operating expenses:		
Research and development	38,034	30,341
General and administrative	15,716	12,927
Total operating expenses	53,750	43,268
Loss from operations	(51,230)	(40,824)
Other income (expense):		
Interest and investment income	2,843	504
Interest expense	(43)	(57)
Other expense	(5)	—
Other income (expense), net	2,795	447
Net loss	$ (48,435)	$ (40,377)
Net loss per share attributable to common shareholders - basic and diluted	$ (2.03)	$ (6.00)
Weighted-average common shares used in computing net loss per share attributable to common shareholders - basic and diluted	23,882,685	6,724,641
Comprehensive loss:		
Net loss	$ (48,435)	$ (40,377)
Net unrealized losses on marketable securities	(56)	(9)
Comprehensive loss	$ (48,491)	$ (40,386)

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Contingently Redeemable Preferred Equity and Stockholders' Equity

(In thousands, except share and unit amounts)

	Contingently redeemable Class A preferred units		Contingently redeemable Series A preferred stock		Class A preferred units		Class B preferred units	
	Units	Amount	Shares	Amount	Units	Amount	Units	Amount
Balance at December 31, 2016	781,693	$ 5,000	—	—	3,922,027	$ 25,548	1,029,850	$ 13,611
Sale of Class B preferred units, net of issuance costs of $18	—	—	—	—	—	—	1,971,717	26,648
Issuance of common stock for license agreement	—	—	—	—	—	—	—	—
Repurchase of founders' units	—	—	—	—	—	—	—	—
Exchange of preferred and common units into preferred and common stock	(781,693)	(5,000)	781,693	5,000	(3,922,027)	(25,548)	(3,001,567)	(40,259)
Sale of Class C preferred stock, net of issuance costs of $1,567	—	—	—	—	—	—	—	—
Convertible preferred stock and contingently redeemable preferred stock exchanged for common stock	—	—	(781,693)	(5,000)	—	—	—	—
Common stock ($.0001 par) exchanged for common stock ($.001 par)	—	—	—	—	—	—	—	—
Issuance of common stock in the Merger	—	—	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	—	—
Issuance of restricted stock	—	—	—	—	—	—	—	—
Cancellation of restricted stock	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—
Effect of adoption of ASU 2016-09	—	—	—	—	—	—	—	—
Unrealized gain/(loss) on securities	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—
Balance at December 31, 2017	—	$ —	—	$ —	—	$ —	—	$ —
Effect of adoption of ASU 2014-09 (ASC 606)	—	—	—	—	—	—	—	—
Sale of common stock	—	—	—	—	—	—	—	—
Exercise of options	—	—	—	—	—	—	—	—
Cancellation of restricted stock	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—
Unrealized gain/(loss) on securities	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—
Balance at December 31, 2018	—	$ —	—	$ —	—	$ —	—	$ —

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Contingently Redeemable Preferred Equity and Stockholders' Equity (continued)

(In thousands, except share and unit amounts)

	Common units		Series A convertible preferred stock		Series B convertible preferred stock		Series C convertible preferred stock	
	Units	Amount	Shares	Amount	Shares	Amount	Shares	Amount
Balance at December 31, 2016	1,847,615	$ 592	—	—	—	—	—	—
Sale of Class B preferred units, net of issuance costs of $18	—	—	—	—	—	—	—	—
Issuance of common stock for license agreement	179,996	1,750	—	—	—	—	—	—
Repurchase of founders' units	(7,244)	—	—	—	—	—	—	—
Exchange of preferred and common units into preferred and common stock	(2,020,367)	(2,342)	3,922,027	25,548	3,001,567	40,259	—	—
Sale of Class C preferred stock, net of issuance costs of $1,567	—	—	—	—	—	—	2,882,679	40,433
Convertible preferred stock and contingently redeemable preferred stock exchanged for common stock	—	—	(3,922,027)	(25,548)	(3,001,567)	(40,259)	(2,882,679)	(40,433)
Common stock ($.0001 par) exchanged for common stock ($.001 par)	—	—	—	—	—	—	—	—
Issuance of common stock in the Merger	—	—	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	—	—
Issuance of restricted stock	—	—	—	—	—	—	—	—
Cancellation of restricted stock	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—
Effect of adoption of ASU 2016-09	—	—	—	—	—	—	—	—
Unrealized gain/(loss) on securities	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—
Balance at December 31, 2017	—	$ —	—	$ —	—	$ —	—	$ —
Effect of adoption of ASU 2014-09 (ASC 606)	—	—	—	—	—	—	—	—
Sale of common stock	—	—	—	—	—	—	—	—
Exercise of options	—	—	—	—	—	—	—	—
Cancellation of restricted stock	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—
Unrealized gain/(loss) on securities	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—
Balance at December 31, 2018	—	$ —	—	$ —	—	$ —	—	$ —

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Contingently Redeemable Preferred Equity and Stockholders' Equity (continued)

(In thousands, except share and unit amounts)

	Common stock $0.0001 par		Common stock $0.001 par		Additional paid-in	Unrealized gain/(loss) on	Accumulated	Total
	Shares	Amount	Shares	Amount	capital	securities	deficit	equity
Balance at December 31, 2016	—	—	—	—	—	—	$ (31,248)	$ 8,503
Sale of Class B preferred units, net of issuance costs of $18	—	—	—	—	—	—	—	26,648
Issuance of common stock for license agreement	—	—	—	—	—	—	—	1,750
Repurchase of founders' units	—	—	—	—	—	—	—	—
Exchange of preferred and common units into preferred and common stock	2,020,367	—	—	—	2,342	—	—	—
Sale of Class C preferred stock, net of issuance costs of $1,567	—	—	—	—	—	—	—	40,433
Convertible preferred stock and contingently redeemable preferred stock exchanged for common stock	—	—	10,587,966	10	111,230	—	—	5,000
Common stock ($.0001 par) exchanged for common stock ($.001 par)	(2,714,694)	—	2,714,694	3	(3)	—	—	—
Issuance of common stock in the Merger	—	—	2,979,836	3	40,430	—	—	40,433
Exercise of stock options	—	—	386	—	5	—	—	5
Issuance of restricted stock	697,292	—	2,884	—	—	—	—	—
Cancellation of restricted stock	(2,965)	—	(13,149)	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	2,652	—	—	2,652
Effect of adoption of ASU 2016-09	—	—	—	—	29	—	(29)	—
Unrealized gain/(loss) on securities	—	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—	—	(40,377)	(40,377)
Balance at December 31, 2017	—	$ —	16,272,617	$ 16	$ 156,685	$ (9)	$ (71,654)	$ 85,038
Effect of adoption of ASU 2014-09 (ASC 606)	—	—	—	—	—	—	324	324
Sale of common stock	—	—	9,179,500	9	82,657	—	—	82,666
Exercise of options	—	—	19,830	—	244	—	—	244
Cancellation of restricted stock	—	—	(70,468)	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	4,317	—	—	4,317
Unrealized gain/(loss) on securities	—	—	—	—	—	(56)	—	(56)
Net loss	—	—	—	—	—	—	(48,435)	(48,435)
Balance at December 31, 2018	—	$ —	25,401,479	$ 25	$ 243,903	$ (65)	$ (119,765)	$ 124,098

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31, 2018	Year Ended December 31, 2017
Cash flows from operating activities:		
Net loss	$ (48,435)	$ (40,377)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	2,421	2,310
Loss on disposal of property and equipment	8	5
Equity-based compensation expense	4,317	2,652
Common shares issued for license acquisition	—	1,750
Accretion/amortization of investment securities	(1,401)	(6)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(45)	(87)
Accounts payable and accrued expenses	(257)	4,071
Deferred revenue	(520)	(444)
Deferred rent	1,274	(1,121)
Other assets	168	192
Net cash, cash equivalents and restricted cash used in operating activities	(42,470)	(31,055)
Cash flows from investing activities:		
Net assets acquired in reverse merger, net of transaction costs	—	40,433
Purchases of marketable securities	(172,887)	(51,438)
Proceeds from maturity of marketable securities	91,340	22,850
Proceeds from sale of property and equipment	—	11
Purchases of property and equipment	(5,654)	(2,578)
Net cash, cash equivalents and restricted cash (used in) provided by investing activities	(87,201)	9,278
Cash flows from financing activities:		
Payments on capital lease obligations	(427)	(408)
Proceeds from exercise of stock options	244	5
Proceeds from sale of common stock, net of issuance costs	82,666	—
Proceeds from sale of convertible preferred stock, net of issuance costs	—	40,433
Proceeds from sale of preferred units, net of issuance costs	—	26,648
Net cash, cash equivalents and restricted cash provided by financing activities	82,483	66,678
Net (decrease) increase in cash, cash equivalents and restricted cash	(47,188)	44,901
Cash, cash equivalents and restricted cash at beginning of period	59,537	14,636
Cash, cash equivalents and restricted cash at end of period	$ 12,349	$ 59,537
Supplemental disclosure of non-cash investing activities:		
Landlord funded allowance for tenant improvements	$ 1,654	$ 4,961
Property and equipment purchases included in accounts payable and accrued expenses	$ 169	$ 147
Supplemental disclosure of non-cash financing activities:		
Cash paid for interest	$ 43	$ 35
Purchase under capital lease	$ 12	$ 918
Prior period adjustment related to the adoption of ASU 2016-09	$ —	$ 29

See accompanying notes to the consolidated financial statements.

(1) Nature of Business

Organization

Synlogic, Inc., together with its wholly owned and consolidated subsidiaries ("Synlogic" or the "Company"), is a clinical-stage biopharmaceutical company focused on advancing its drug discovery and development platform for Synthetic Biotic™ medicines. Synthetic Biotic medicines are generated from Synlogic's proprietary drug discovery and development platform applying the principles and tools of synthetic biology to engineer beneficial microbes to perform or deliver critical therapeutic functions to treat metabolic and inflammatory diseases and cancer. As living medicines, Synthetic Biotic medicines can be designed to sense a local disease context within a patient's body and to respond by metabolizing a toxic substance, compensating for missing or damaged metabolic pathways in patients, or by delivering combinations of therapeutic factors. Synlogic's goal is to lead in the discovery and development of Synthetic Biotic therapies as living medicines capable of robust and precise pathway complementation and delivery of therapeutic benefit. Since incorporation, the Company has devoted substantially all of its efforts to the research and development of its product candidates.

Synlogic, Inc. ("Private Synlogic" when referred to prior to the Merger (as defined below)) was founded and began operations on March 14, 2014, as TMC Therapeutics, Inc., located in Cambridge, Massachusetts. On July 15, 2014, TMC Therapeutics, Inc. changed its name to Synlogic, Inc. On July 2, 2015, the common and preferred stockholders of Private Synlogic executed the Synlogic, LLC Contribution Agreement (the "Contribution Agreement"), pursuant to which such common and preferred stockholders contributed such stockholders' equity interests in Private Synlogic in exchange for common and preferred units in a newly formed parent company named Synlogic, LLC. In addition, Synlogic IBDCo, Inc. ("IBDCo") was formed as a subsidiary of Synlogic, LLC (the "2015 Reorganization"). In conjunction with the 2015 Reorganization, Private Synlogic entered into a license, option and merger agreement with AbbVie S.à.r.l. ("AbbVie"), for the development of treatments for inflammatory bowel disease ("IBD").

In May 2017, Private Synlogic completed a reorganization ("2017 Reorganization") pursuant to which Synlogic, LLC merged with and into Private Synlogic, with Private Synlogic continuing as the surviving corporation. Pursuant to the 2017 Reorganization, the common units and preferred units of Synlogic, LLC, together consisting of Class A preferred units, contingently redeemable Class A preferred units and Class B preferred units, were exchanged for common stock and preferred stock of Private Synlogic, respectively. Additionally, Private Synlogic issued equity awards under the Synlogic 2017 Stock Incentive Plan ("2017 Plan") to replace the canceled incentive units pursuant to the termination of the Synlogic, LLC 2015 Equity Incentive Plan ("2015 LLC Plan").

On August 28, 2017, Synlogic, Inc., formerly known as Mirna Therapeutics, Inc. (NASDAQ: MIRN) ("Mirna"), completed its business combination with Private Synlogic pursuant to 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"). Immediately after completion of the Merger, Mirna changed its name to "Synlogic, Inc." (NASDAQ: SYBX).

Risks and Uncertainties

At December 31, 2018, the Company had approximately $122.7 million in cash, cash equivalents, and marketable securities, approximately $1.1 million of restricted cash, and an accumulated deficit of approximately $119.8 million. Since its inception through December 31, 2018, the Company has primarily financed its operations through the issuance of preferred stock and units, the sale of its common stock, the AbbVie collaboration, and cash received in the Merger. In the absence of positive cash flows from operations, the Company is highly dependent on its ability to find additional sources of funding in the form of debt or equity financing. In January 2018, the Company sold shares of its common stock in a firm commitment, underwritten public offering and received $53.8 million in net proceeds from this offering, after underwriting discounts and commissions and other offering expenses. In April 2018, the Company sold shares of its common stock in a registered direct offering and received $28.9 million in net proceeds from this offering, after fees and other expenses. Management believes that the Company has sufficient cash to fund its operations through at least twelve months from the issuance of these financial statements.

As an early-stage company, the Company is subject to a number of risks common to other life science companies, including, but not limited to, raising additional capital, development by its competitors of new technological innovations, risk of failure in preclinical and clinical studies, safety and efficacy of its product candidates in clinical trials, the risk of relying on external parties such as contract research organizations ("CROs") and contract manufacturing organizations ("CMOs"), the regulatory approval process, market acceptance of the Company's products once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. The Company's therapeutic programs are currently pre-commercial, spanning discovery through early development and will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel, infrastructure, and extensive compliance-reporting capabilities. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate revenue from product sales. The Company may never achieve profitability, and unless and until it does, it will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or partnerships.

(2) Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S.") ("U.S. GAAP" or "GAAP").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Synlogic and its wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in accordance with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. On an on-going basis, the Company's management evaluates its estimates, including those related to revenue recognition, income taxes including the valuation allowance for deferred tax assets, research and development accruals, accrued expenses, contingencies and equity-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Cash Equivalents

The Company considers all highly liquid investment instruments with a remaining maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents primarily consist of money market funds and corporate debt securities. Cash equivalents are stated at cost plus accrued interest, which approximates fair value. The amount of cash equivalents included in cash and cash equivalents was approximately $0.3 million and $32.7 million at December 31, 2018 and 2017, respectively.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk include amounts held as cash, cash equivalents, marketable securities and restricted cash. The Company uses high quality, accredited financial institutions to maintain its balances, and accordingly, such funds are subject to minimal credit risk. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no financial instruments with off-balance sheet risk of loss.

Restricted Cash

The Company held cash of approximately $1.0 million at December 31, 2018 in a letter of credit to secure its lease at the 301 Binney Street facility. In addition, the Company held cash of $50,000 at December 31, 2018 and 2017 in a separate restricted bank account as collateral for the Company's credit cards. The Company has classified these deposits as long-term restricted cash on its balance sheet.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows (in thousands).

	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 11,252	$ 58,440
Restricted cash included in other long-term assets	1,097	1,097
Total cash, cash equivalents, and restricted cash shown in the consolidated statement of cash flows	$ 12,349	$ 59,537

Fair Value

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. Accounting Standards Codification ("ASC") Topic 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

- Level 1 – Utilize observable inputs such as quoted prices in active markets for identical assets or liabilities;
- Level 2 – Utilize data points that are either directly or indirectly observable, such as quoted prices, interest rates and yield curves;
- Level 3 – Utilize unobservable data points in which there is little or no market data, which require the Company to develop its own assumptions for the asset or liability.

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1, Level 2 or Level 3 during the years ended December 31, 2018 and 2017.

Available-for-Sale Securities

The Company classifies all short-term investments with an original maturity when purchased of greater than three months as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in other comprehensive income (loss). The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, and declines in value judged to be other than temporary on available-for-sale securities, are included in interest and investment income.

The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest and investment income. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary.

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Repairs and maintenance costs are expensed as incurred, whereas major improvements are capitalized as additions to property and equipment.

Depreciation begins at the time the asset is placed in service. Depreciation is provided over the following estimated useful lives:

Asset classification	Useful life
Computer and office equipment	3 years
Furniture and fixtures	5 years
Laboratory equipment	5 years
Leasehold improvements	Lesser of useful life or remaining lease term

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If this comparison indicates that there is impairment, the amount of impairment is calculated as the difference between the carrying value and fair value of the asset. To date, no such impairments have been recognized.

Rent Expense

The Company's leases for both the 301 Binney Street facility and the 200 Sidney Street facility in Cambridge, Massachusetts provide for a rent-free period as well as fixed increases in minimum annual rental payments. The total amount of rental payments due over the lease term is being charged to rent expense on a straight-line basis over the term of the lease. Tenant improvement allowances and other incentives are recorded as deferred rent and amortized as a reduction of periodic rent expense, over the term of the lease. Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the Company's facilities. The Company began to accelerate the recognition of deferred rent on its 200 Sidney Street facility when it agreed to terminate the lease in July 2017.

Research and Development Costs

Costs incurred in the research and development of the Company's product candidates are expensed as incurred. The Company defers and capitalizes nonrefundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary and benefits, equity-based compensation expense, laboratory supplies and other direct expenses, facilities expenses, overhead expenses, contractual services and other outside expenses.

When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial costs, contractual services costs and costs for supply of its drug candidates, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period and the expected duration of the third-party service contract, where applicable.

Revenue recognition

The Company generates revenue through a collaboration and license arrangement with a strategic partner for the development and commercialization of product candidates.

Effective January 1, 2018, the Company adopted ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606") using the modified retrospective transition method. Refer to the Recently Adopted Accounting Pronouncements section below for additional information on the new standard and the impact to our results of operations. Under this method, results for reporting periods beginning after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605").

The Company evaluates collaboration agreements with respect to FASB ASC Topic 808, *Collaborative Arrangements*, considering the nature and contractual terms of the arrangement and the nature of its business operations to determine the classification of the transactions. When the Company is an active participant in the activity and exposed to significant risks and rewards dependent on the commercial success of the collaboration, it will record its transactions on a gross basis in the consolidated financial statements and describe the rights and obligations under the collaborative arrangement in the notes to the consolidated financial statements.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five-step analysis: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step analysis to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company may enter into collaboration agreements for research and development services, under which the Company may license certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees; reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Variable consideration is constrained until it is deemed not be at significant risk of reversal.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements for which the collaboration partner is also a customer, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the contract term and pattern of satisfaction of the performance obligations under step (v) above. The Company uses significant judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to the goods and services the Company expects to provide. The Company uses estimates to determine the timing of satisfaction of performance obligations, which may include the use of full time equivalent time as a measure of satisfaction of performance obligations.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Licenses of Intellectual Property

In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and Development Services

If an arrangement is determined to contain a promise or obligation for the Company to perform research and development services, the Company must determine whether these services are distinct from the other promises in the arrangement. In assessing whether the services are distinct from the other promises, the Company considers the capabilities of the customer to perform these same services. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For research and development services that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer Options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, that is, the option to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on an alternative approach when the goods or services are both (i) similar to the original goods and services in the contract and (ii) provided in accordance with the terms of the original contract. Under this alternative, the Company allocates the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to a material right are not recognized as revenue until the option is exercised and the performance obligation is satisfied.

Milestone Payments

At the inception of each arrangement that includes milestone payments, the Company evaluates whether a significant reversal of cumulative revenue provided in conjunction with achieving the milestones is probable and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, the Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Contract Costs

The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. As a practical expedient, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that we otherwise would have recognized is one year or less. To date, the Company has not incurred any incremental costs of obtaining a contract with a customer.

Equity-Based Compensation

The Company measures equity-based compensation to employees and directors based on the grant date fair value of the awards and recognizes the associated expense in the financial statements over the requisite service period of the award, which is generally the vesting period.

Equity-based compensation costs for nonemployee awards are recognized as services are provided, which is generally the vesting period, on a straight-line basis. The measurement date for nonemployee awards is generally the date the performance of services required from the nonemployee is complete. The Company believes that the fair value of the equity is more reliably measurable than the fair value of the services rendered. The fair value of the award granted to a nonemployee is remeasured at each reporting date until performance is completed with any increase or decrease in fair value recorded as equity-based compensation expense.

Prior to the Merger in August 2017, the Company's Board of Directors determined the estimated per share fair market value of the common stock and common units at various dates considering contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or the Practice Aid. The fair market value of the common stock and common units was determined by the Board of Directors at each award grant date based on assumptions, each of which are subjective and generally require judgement and estimation by management, including results obtained from independent third-party valuations, the Company's financial position and historical financial performance, the status of technological developments within the Company's product candidates, the composition and ability of the research and management team, an evaluation or benchmark of the Company's competition, the business climate in the marketplace, the illiquid nature of the common stock and common units, arm's length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred stock, and the prospects of a liquidity event.

The fair value of each option was estimated on the date of grant or remeasurement using the Black-Scholes option-pricing model. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer-group of similar public companies. The expected term of options granted for employees was calculated using the simplified method, which represented the average of the contractual term of the option and the weighted-average vesting period of the option. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free interest rate is based upon the U.S. Treasury yield curve commensurate with the expected term at the time of grant or remeasurement. Forfeitures are recognized as they occur as allowed under ASU 2016-09.

The Company's Board of Directors estimated the threshold price for each incentive unit issued by Synlogic, LLC, which is the price at which an incentive unit would have had a liquidation value of zero, considering the fair value of the Company's assets at the date of grant and performed an analysis to determine the per unit amount that a holder would have received upon a distribution event. In determining the fair value of its assets, the Company relied on independent third-party valuations, which take into account a variety of factors, including the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the research and management team, an evaluation or benchmark of the Company's competition, the business climate in the marketplace, the illiquid nature of the common units and incentive units, arm's-length sales of the Company's equity, the effect of the rights and preferences of the preferred unit holders, and the prospects of a liquidity event, among others.

The fair value of each incentive unit award was estimated on the date of grant or remeasurement using the Black-Scholes with barrier option-pricing model. Assumptions utilized in the model for valuing the incentive units including expected volatility, dividend yield and risk-free interest rate were arrived at in the same manner as those utilized for the stock option model described above. Forfeitures are treated in the manner described above. Incentive units did not have an expiration date, thus, the expected term of incentive units granted was determined based on the probability-weighted estimated term to a liquidity event.

The Company records the expense for equity grants subject to performance-based milestone vesting over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

The Company classifies equity-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial reporting and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

Uncertain tax positions represent tax positions for which reserves have been established. The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to be recognized in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Net Loss Per Share

Basic net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the sum of the weighted-average number of shares of common stock outstanding during the period and if dilutive, the weighted-average number of potential shares of common stock, including unvested restricted common stock and outstanding stock options.

The Company computed basic and diluted net loss per shares using the two-class method, which gives effect to the impact of the outstanding participating securities. As the years ended December 31, 2018 and 2017 resulted in net losses attributable to common stockholders, there is no income allocation required under the two-class method or dilution attributed to weighted-average shares outstanding in the calculation of diluted net loss per share because the preferred stockholders do not participate in losses of the Company. Accordingly, for periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common stock are not assumed to have been issued if their effect is anti-dilutive.

As the 2017 Reorganization resulted in a one for one conversion of preferred units for preferred stock and common units for common stock, the conversion was not substantive for the purposes of this calculation and the weighted average was calculated as if outstanding equity was outstanding from the beginning of the period presented.

Additionally, at the Effective Time of the Merger, the Company issued shares of its common stock to Private Synlogic stockholders, at the Exchange Ratio of 0.5532 shares of common stock, after taking into account the Reverse Stock Split, in exchange for each share of Private Synlogic preferred and common stock outstanding immediately prior to the Merger. The Exchange Ratio was calculated by a formula pursuant to the Merger Agreement. For the purposes of calculating net loss per share, the Exchange Ratio was applied retroactively to all periods presented.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company operates in one operating segment: discovery and development of synthetic biology therapeutics for the treatment of rare, infectious and other diseases. The Company's chief executive officer, as chief operating decision maker, manages and allocates resources to the operations of the Company on a total company basis. All of the Company's equipment, leasehold improvements and other fixed assets are physically located within the United States, and all agreements with its partners are denominated in U.S. dollars, except where noted.

Recently Adopted Accounting Pronouncements

Revenue Recognition

In May 2014, the FASB, issued Accounting Standards Update, (ASU), No. 2014-09, which amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in ASC 605 and creates ASC 606. In 2015 and 2017, the FASB issued additional ASUs related to ASC 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements and practical expedients.

Effective January 1, 2018, the Company adopted ASC 606 using the modified retrospective transition method. Under this method, results for reporting periods beginning after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance and financial instruments. As a result of adopting ASC 606 on January 1, 2018, the Company recorded a cumulative-effect decrease to opening accumulated deficit of $0.3 million as of January 1, 2018 and a corresponding decrease to deferred revenue. Total revenue recorded in the twelve months ended December 31, 2018 under ASC 606 was $2.5 million, as compared to $2.4 million that would have been recorded under ASC 605. Deferred revenue as of December 31, 2018 was $0.3 million under ASC 606, as compared to a balance of $0.7 million which would have resulted under ASC 605.

The most significant changes relate to the Company's revenue recognition pattern for the AbbVie collaboration and the accounting for milestone payments. Under ASC 605, the Company was recognizing the revenue allocated to each unit of accounting on a straight line basis over the period the Company is expected to complete its obligations. Under ASC 606, the Company is recognizing the revenue allocated to each performance obligation measuring progress using an input method over the period the Company is expected to complete each performance obligation. Under ASC 605, the Company recognized revenue related to milestone payments as the milestone was achieved, using the milestone method. Under ASC 606, the Company determined that the milestones at the beginning of certain research and development phases represent a 90-day contract with daily customer renewal options for the Company's continued research and development services. As a result, revenue from these milestones is recognized over a performance obligation consisting of the next phase of research and development services.

Income Taxes

In March 2018, the FASB issued Accounting Standards Update No. 2018-05, Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118 ("ASU 2018-05"). The standard amends ASC 740, Income Taxes ("ASC 740"), to provide guidance on accounting for the tax effects of the Tax Act pursuant to Staff Accounting Bulletin No. 118, effective immediately. The ASU permits companies to use provisional amounts for certain income tax effects of the Tax Act during a one-year measurement period. The provisional reporting period ended on December 22, 2018 and no further adjustment was required for the year ended December 31, 2018.

Stock Compensation

In May 2017, the FASB issued ASU 2017-09, Compensation – Stock Compensation (Topic 718): Scope of Modification Accounting. The new standard is intended to reduce the diversity in practice, cost and complexity when applying the guidance in Topic 718 to a change to the terms or conditions of a share-based payment award. The new standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2018. The amendments in this update will be applied prospectively to an award modified on or after the adoption date. The Company adopted this standard as of January 1, 2018 and it did not have a material impact on the Company's financial position or results of operations.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02 – Leases (Topic 842), which replaces the existing accounting guidance for leases. This standard requires entities that lease assets to recognize the assets and liabilities for the rights and obligations created by those leases on the balance sheet. The standard is effective for fiscal years and the interim periods within those fiscal years beginning after December 15, 2018. The guidance is required to be applied by the modified retrospective transition approach and early adoption is permitted. In July 2018, the FASB issued ASU 2018-11 Leases – Targeted Improvements, intended to ease the implementation of the new lease standard for financial statement preparers by, among other things, allowing for an additional transition method. In lieu of presenting transition requirements to comparative periods, as previously required, an entity may now elect to show a cumulative effect adjustment on the date of adoption without the requirement to recast prior period financial statements or disclosures presented in accordance with ASU 2016-02. We expect to adopt the new standard and elect to use the cumulative effect adjustment transition option effective January 1, 2019, which will be the initial date of application per ASU 2018-11.

The Company expects to elect the available package of practical expedients which allows us to not reassess previous accounting conclusions around whether arrangements are or contain leases, the classification of our leases, and the treatment of initial direct costs. The Company also expects it will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. The Company is continuing to evaluate developments within the new lease guidance and is finalizing its evaluation of its existing population of contracts to ensure all contracts that meet the definition of a lease contract under the new standard are identified. The Company has assessed the impact that the adoption of this guidance will have on its financial statements and footnote disclosures. The standard will have a material impact on the consolidated balance sheet related to the recognition of right-of-use assets and lease liabilities for operating leases. The standard will not have a material impact on the consolidated statement of operations. The Company has designed and implemented changes to related processes, controls and disclosures.

In February 2018, the FASB issued ASU 2018-02 – Income Statement – Reporting Comprehensive Income (Topic 220), which provides amended guidance on income tax accounting. The amended guidance permits the reclassification of the income tax effect on amounts recorded within other comprehensive income impacted by the Tax Cuts and Jobs Act into retained earnings. The amended guidance is effective for periods beginning after December 15, 2018 and applies only to those amounts remaining in Other Comprehensive Income at the date of enactment of the Act. The amended guidance may be adopted on either a retrospective basis or at the beginning of the period of adoption. The Company is assessing the potential impact of the amended standard but does not expect it to have a material impact on its consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07 – Compensation –Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The standard is effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of ASC 606. The standard expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. Under the amended guidance, equity-classified share-based payment awards issued to nonemployees will be measured at grant date fair value. Upon transition, the entity is required to remeasure these nonemployee awards at fair value as of the adoption date. The Company is currently evaluating the new guidance but does not expect it to have a material impact on its consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13 - Fair Value Measurement - Disclosure Framework (Topic 820). The standard modifies the disclosure requirements for fair value measurements. The standard is effective for public companies for annual and interim periods beginning after December 15, 2019. Early adoption is permitted for any removed or modified disclosures. Management is currently assessing the impact adoption will have on the Company, but it is not expected to have a material impact on the Company's financial statement disclosures.

In August 2018, the FASB issued ASU 2018-15 - Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement that is a Service Contract. The standard requires implementation costs incurred by customers in cloud computing arrangements to be deferred over the noncancelable term of the cloud computing arrangements plus any optional renewal periods (1) that are reasonably certain to be exercised by the customer or (2) for which exercise of the renewal option is controlled by the cloud service provider. The effective date of this pronouncement is for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years, and early adoption is permitted. The standard can be adopted either using the prospective or retrospective transition approach. The Company is currently evaluating the impact of this pronouncement on the Company's consolidated financial statements and disclosures.

In November 2018, the FASB issued ASU 2018-18 - Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606, which, among other things, provides guidance on how to assess whether certain collaborative arrangement transactions should be accounted for under Topic 606. The amendments in this ASU are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019, with early adoption permitted. The Company is in the process of evaluating the impact the standard will have on its financial statements.

(3) Merger with Mirna Therapeutics

On August 28, 2017, Private Synlogic completed the Merger with Mirna as discussed in Note 1. For accounting purposes, Private Synlogic is considered to have acquired Mirna in the Merger. Private Synlogic was determined to be the accounting acquirer based upon the terms of the Merger and other factors including: (i) Private Synlogic stockholders owned approximately 83% of the combined company immediately following the closing of the Merger, (ii) Private Synlogic directors held five of the seven board seats in the combined company, and (iii) Private Synlogic management held all key positions in the management of the combined company. The Merger was accounted for as an asset acquisition rather than a business combination because the assets acquired and liabilities assumed by the Company do not meet the definition of a business as defined by ASC Topic 805, *Business Combinations*. The net assets acquired in connection with this transaction were recorded at their estimated acquisition date fair values as of August 28, 2017, the date the Merger was completed (the "Merger Closing Date").

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. Mirna assumed all of the stock options outstanding under the 2017 Plan, with such stock options henceforth representing the right to purchase a number of shares of Mirna's common stock equal to the Exchange Ratio multiplied by the number of shares of Private Synlogic common stock previously represented by such options. Mirna also assumed the 2017 Plan. The consolidated financial statements give retroactive effect to the Exchange Ratio for all periods presented.

On the Merger Closing Date, Mirna had approximately 20.9 million shares of common stock outstanding and a market capitalization of approximately $35.0 million. The estimated fair value of the net assets of Mirna on August 28, 2017 was approximately $42.6 million. The fair value of the Mirna common stock on the Merger Closing Date was below the fair value of Mirna's net assets. As Mirna's net assets were predominantly comprised of cash, cash equivalents and marketable securities, partially offset by current liabilities, the fair value of Mirna's net assets as of the Merger Closing Date is considered to be the best indicator of the fair value and, therefore, the estimated preliminary purchase consideration.

All of Mirna's assets and liabilities were reflected at their fair value on the Merger Closing Date. No goodwill or intangible assets were recognized. Consistent with accounting for an asset acquisition, the Company capitalized the costs associated with the Merger. Transaction costs primarily included bank fees and professional fees associated with legal counsel, auditors and printers. The following table shows the net assets acquired in the Merger (in thousands):

	August 28, 2017
Cash and cash equivalents	$ 14,882
Marketable securities	27,600
Interest receivable	126
Prepaid assets	112
Unrealized loss on marketable securities	5
Accounts payable and accrued expenses	(105)
Total net assets acquired	42,620
Less: Transaction costs	(2,187)
Total net assets acquired less transaction costs	$ 40,433

(4) Fair Value of Financial Instruments

The tables below present information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2018 and 2017 and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value, as described under Note 2*, Summary of Significant Accounting Policies*.

The Company's investment portfolio includes many fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company applied other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare evaluations. In addition, model processes were used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data.

At December 31, 2018 and 2017, the Company has classified assets measured at fair value on a recurring basis as follows (in thousands):

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds (included in cash and cash equivalents)	$ 265	$ 265	$ —	$ —
Corporate debt securities (included in short-term investments)	107,505	—	107,505	—
U.S. government agency securities and treasuries (included in short-term investments)	3,972	1,987	1,985	—
Total	$ 111,742	$ 2,252	$ 109,490	$ —

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds (included in cash and cash equivalents)	$ 21,301	$ 21,301	$ —	$ —
Corporate debt securities (included in cash and cash equivalents)	11,405	—	11,405	—
Corporate debt securities (included in short-term investments)	28,585	—	28,585	—
Total	$ 61,291	$ 21,301	$ 39,990	$ —

Cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses at December 31, 2018 and December 31, 2017 are carried at amounts that approximate fair value due to their short-term maturities. Capital lease obligations at December 31, 2018 and December 31, 2017 approximate fair value as they bear interest at a rate approximating a market interest rate.

(5) Available-for-Sale Investments

The following tables summarize the available-for-sale securities held at December 31, 2018 and 2017 (in thousands):

December 31, 2018	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Corporate debt securities	$ 107,571	$ 4	$ (70)	$ 107,505
U.S. government agency securities	$ 3,971	$ 1	$ —	$ 3,972
Total	$ 111,542	$ 5	$ (70)	$ 111,477

December 31, 2017	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Corporate debt securities	$ 28,593	$ 1	$ (9)	$ 28,585
Total	$ 28,593	$ 1	$ (9)	$ 28,585

The contractual maturity of all securities held at December 31, 2018 was one year or less. There were 37 investments in an unrealized loss position at December 31, 2018, none of which had been in an unrealized loss position for more than twelve months. The aggregate fair value of the securities in an unrealized loss position at December 31, 2018 and 2017 was $96.5 million and $19.3 million, respectively. The Company reviews its investments for other-than-temporary impairment whenever the fair value of an investment is less than amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company did not hold any securities with an other-than-temporary impairment at December 31, 2018.

Gross realized gains and losses on the sales of investments have not been material to the Company's consolidated statement of operations.

(6) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consists of the following (in thousands):

	December 31, 2018	December 31, 2017
Prepaid insurance	$ 502	$ 437
Prepaid research and development	122	508
Other prepaid	597	321
Other current assets	388	298
	$ 1,609	$ 1,564

(7) Property and Equipment, net

Property and equipment, net consists of the following (in thousands):

	December 31, 2018	December 31, 2017
Laboratory equipment	$ 7,111	$ 2,999
Computer and office equipment	781	354
Furniture and fixtures	413	220
Leasehold improvements	9,484	2,308
Construction in progress	39	7,017
	17,828	12,898
Less accumulated depreciation	(2,987)	(3,115)
	$ 14,841	$ 9,783

At December 31, 2018 and 2017, leasehold improvements include approximately $6.6 million and $1.3 million, respectively, of lessor-paid tenant improvements for which the Company was deemed to be the accounting owner of the tenant improvements primarily because it was responsible for project cost overruns. Also, at December 31, 2017, construction in progress contained approximately $5.0 million of lessor-paid tenant improvements placed in service in 2018, for which the Company was deemed to be the accounting owner primarily because it was responsible for project cost overruns.

In both 2018 and 2017, the Company entered into leases for certain laboratory equipment which were capital leases. The leases had either a present value of expected payments in excess of 90% of the fair value of the equipment or a bargain purchase option at the end of the lease. As such, as of December 31, 2018 and 2017, the Company had approximately $1.3 million and $1.4 million, respectively, of assets under a capital lease having accumulated depreciation of approximately $0.9 million and $0.2 million, respectively.

(8) Accrued Expenses

Accrued expenses consists of the following (in thousands):

	December 31, 2018	December 31, 2017
Payroll related	$ 2,906	$ 1,721
Professional fees	306	805
Research and development	1,585	2,027
Other	237	270
	$ 5,034	$ 4,823

(9) Common Stock

The Company's common stock has the following characteristics:

- The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders.
- The holders of shares of common stock are entitled to receive dividends, if and when, declared by the Company's board of directors. Since inception, no cash dividends have been declared.

The Company holds forfeiture rights relating to 118,679 shares of common stock. The forfeiture right lapses over time and is triggered when a holder ceases providing services to the Company. As of December 31, 2018, 86,581 shares of common stock have been forfeited back to the Company.

The Company holds repurchase rights which are at a price equal to the initial purchase price by the founders of Private Synlogic, adjusted by the Merger Exchange Ratio. The repurchase right lapses over time and is exercisable should the founders cease providing services to the Company prior to the end of a four-year period which began in April or May 2014, as the case may be. All repurchase

rights terminated during 2018. As of December 31, 2018, the Company has exercised its repurchase right on 41,819 shares of common stock.

In January 2018, the Company sold 5,899,500 shares of its common stock through a firm commitment, underwritten public offering at a price to the public of $9.75 per share. As a result of the offering, including the exercise of the overallotment option, the Company received aggregate net proceeds, after underwriting discounts and commissions and other estimated offering expenses, of approximately $53.8 million.

In April 2018, the Company sold 3,280,000 shares of its common stock at a price of $9.15 per share in a registered direct offering. After fees and other offering expenses, the Company received approximately $28.9 million in net proceeds from the offering.

(10) Preferred Stock

Preferred Stock of Synlogic, Inc.

The Company's preferred stock may be issued from time to time in one or more series, with each such series to consist of such number of shares and to have such terms as adopted by the board of directors. Authority is given to the board of directors to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitation or restrictions thereof, including without limitation, dividend rights, conversion rights, redemption privileges and liquidation preferences.

Preferred Stock of Private Synlogic

Prior to the Merger, Private Synlogic had contingently redeemable preferred stock and three series of convertible preferred stock. On the Merger Closing Date, Mirna issued shares of its common stock to holders of these shares, at an exchange rate of 0.5532 shares of common stock, after taking into account the Reverse Stock Split, in exchange for each share of preferred stock outstanding immediately prior to the Merger.

Pursuant to, and at the time of, the 2017 Reorganization, preferred stock was granted to all holders of preferred units. The Synlogic preferred stock had substantially similar rights and preferences as the preferred units, except that the preferred stock was convertible into common stock at the option of the holder, on a one-for-one basis, subject to an antidilution adjustment. Conversion of the preferred stock would have been automatically triggered upon a firm-commitment underwritten public offering or upon a supermajority preferred interest vote (see (a)(v) below).

After the 2017 Reorganization, in May 2017, the Company sold and issued 2,882,679 shares of Series C preferred stock at $8.06 per share to investors for total consideration of approximately $40.4 million, net of offering costs of approximately $1.6 million. The Series C preferred stock was issued with the same terms as the then-existing preferred stock.

Rights and Preferences

Preferred stock had the following rights and preferences:

(i) Voting

The holders of the preferred stock were entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote, except with respect to matters on which Delaware General Corporation Law required that a vote would be by a separate class, in which case the holders of the preferred stock would have voted separately as a class. Each holder of preferred stock was entitled to the number of votes equal to the number of shares of common stock into which each share of preferred stock was convertible at the time of such vote.

(ii) Dividends

In the event that a dividend was declared for the holders of common stock, the holders of the preferred stock would have been entitled to the amount of dividends on an as-converted basis. Through December 31, 2018 and December 31, 2017, no dividends were declared or paid.

(iii) Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of shares of preferred stock then outstanding would have been entitled to be paid, on a pari passu basis, out of the assets of the Company available for distribution to its stockholders before any payment was made to the holders of common stock by reason of their ownership thereof, with respect to each series of preferred stock, an amount per share equal to the greater of (i) the applicable original issue price, plus any dividends declared but unpaid thereon, or (ii) such amount per share as would have been payable had all shares been converted into common stock immediately prior to such liquidation, dissolution or winding up of the Company.

If upon any such liquidation, dissolution or winding up of the Company, the assets of the Company available for distribution to its stockholders were insufficient to pay the holders of shares of preferred stock the full amount to which they should have been entitled, the holders of shares of preferred stock would share ratably in any distribution of the assets available for distribution in proportion to the respective amounts that would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

(iv) Par Value

Par value was assigned as $0.0001.

(v) Conversion

Each share of preferred stock, at the option of the holder, was convertible into that number of fully paid shares of common stock as determined by dividing the sum of the original issue price, plus any declared but unpaid dividends, by the conversion price in effect at the time of conversion. The initial conversion price for each share of preferred stock would have been the original issue price, subject to adjustment in accordance with antidilution provisions. Each share of preferred stock would have been automatically converted upon (i) the closing of a firm commitment underwritten public offering in which the public offering price exceeded $12.09 (adjusted to reflect subsequent stock dividends, stock splits or recapitalization) and the aggregate proceeds raised were not less than $50,000,000, or (ii) upon the vote or written consent of a supermajority preferred interest (or a majority preferred interest in the event of a public offering that did not result in the offering price or aggregate proceeds amount set forth in clause (i) above).

(vi) Redemption

The preferred stock was not redeemable except upon a deemed liquidation event. Deemed liquidation events included a merger or acquisition in which the majority of the stock of the pre-merger corporation was not owned by the majority of the stockholders of the post-merger entity or the sale of all or substantially all of the Company's assets. All holders of equally and more subordinated equity instruments of the Company would have been entitled to receive the same form of consideration upon the occurrence of a deemed liquidation event, consequently, the preferred stock was classified as permanent equity.

In September 2014, the Company entered into a letter agreement with the Bill & Melinda Gates Foundation ("the Gates Foundation") with respect to the Gates Foundation purchase of 781,693 shares of the Company's Series A Preferred Stock. The Gates Foundation investment was made in three tranches of 201,163 shares in September 2014, 218,646 shares in May 2015 and 361,884 shares in February 2016. Under the letter agreement, the Company was required to spend the approximately $5.0 million invested by the Gates Foundation for research on a particular disease, further develop the Company's proprietary technology platform and provide assistance with access to use of such technology in developing countries. If the Company failed to spend the amount appropriately, or defaulted under certain other commitments in the agreement and the Company did not cure such default within 90 days of notice, if requested by the Gates Foundation, the Company would have been obligated to redeem the shares of Series A Preferred Stock or shares of common stock into which they had converted then held by the Gates Foundation or find a third-party to purchase such shares at a price equal to the greater of the initial purchase price and the then current fair value of such shares. In either case, if the Company, over the 6 months following such redemption, had sold substantially all of its equity or assets or completed an initial public offering at a value greater than 200% of the price paid upon redemption, then the Company would have had to reimburse the Gates Foundation for the difference. As of December 31, 2017, all obligations with respect to the Gates Foundation investment have been satisfied.

Participation Rights in Future Equity Issuances

For series of preferred stock that were issued in multiple tranches, all holders of preferred stock had a pro rata right and obligation, based on their percentage equity ownership within the series, to participate in subsequent issuances within the same series of equity securities of the Company approved by 70% vote of holders of preferred stock. Should any such holder have chosen not to purchase its full pro rata share, they would have been deemed a defaulting purchaser and all preferred stock held by a defaulting purchaser would have been automatically converted into common stock of the Company.

(11) Preferred Units

Prior to the 2017 Reorganization, the Company had one class of contingently redeemable preferred units and two classes of convertible preferred units. Pursuant to the 2015 Reorganization, each share of the Company's Series A Preferred Stock and Series A Contingently Redeemable Preferred Stock was exchanged for a like type and number of the Company's Class A Preferred Units and Contingently Redeemable Class A Preferred Units, respectively.

In February 2016, Synlogic issued and sold 2,005,348 units of Class A-3 Preferred Units and 361,884 units of Contingently Redeemable Class A-3 Preferred Stock at $7.23 per unit to investors for net proceeds of approximately $17.1 million. There were no issuance costs related to these transactions.

In February 2016, Synlogic also issued and sold 1,029,850 units of Class B Preferred Units at $13.53 per unit to investors for net proceeds of approximately $13.6 million. Issuance costs related to this transaction of approximately $0.3 million were recorded as a reduction of proceeds within Class B Preferred Units (together with the Class A Preferred Units, Contingently Redeemable Class A Preferred Units, Class A-2 Preferred Units, Class A-2 Contingently Redeemable Preferred Units, Class A-3 Preferred Units and Contingently Redeemable Class A-3 Preferred Units, the "Preferred Units").

Rights and Preferences

The Preferred Units had substantially similar rights and preferences as were conferred upon the preferred stock as follows:

(i) Voting

The holders of the Preferred Units were entitled to vote, together with the holders of the Company's common units as a single class, on all matters submitted to unit holders for a vote. In addition, holders of at least a majority of the outstanding Preferred Units and common units voting as a single class were entitled to take any action required or permitted to be taken at any meeting of the members, unless a different vote is required by the Delaware Limited Liability Company Act or the Company's operating agreement.

(ii) Distributions

Distributions were governed by the Company's operating agreement (Note 13). No distributions were made in either of the years ended December 31, 2018 or December 31,2017.

(iii) Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the assets of the Company would have been distributed, after the payout or provision for payment of all creditors of the Company, in accordance with the same order of priority as distributions (Note 13).

(iv) Par Value

The Preferred Units did not have a par value.

(v) Redemption

The Preferred Units were not redeemable except upon a deemed liquidation event. Deemed liquidation events included the merger, acquisition or sale of all or substantially all of the Company's assets. All holders of equally and more subordinated equity instruments of the Company would have been entitled to receive the same form of consideration upon the occurrence of a deemed liquidation event, consequently, the Preferred Units were classified as permanent equity.

In September 2014, the Company entered into a letter agreement with the Bill & Melinda Gates Foundation ("the Gates Foundation") (Note 10) with respect to the Gates Foundation purchase of 781,693 shares of the Company's Series A Preferred Stock. The Gates Foundation investment was made in three tranches of 201,163 shares in September 2014, 218,646 shares in May 2015 and 361,884 units in February 2016. The first two tranches, totaling 419,809 shares were exchanged for Class A Preferred Units pursuant to the 2015 Reorganization in July 2015. As a result, 781,693 units of Class A Preferred Units with a cost of approximately $5.0 million were classified as Contingently Redeemable Preferred Units in mezzanine equity, as of December 31, 2016.

(vi) Participation Rights

Holders of Class A Preferred Units had the right and obligation to participate in additional closings of Class A Preferred Units upon the achievement of certain milestones by the Company. If any holder of Class A Preferred Units did not purchase the number of Class A Preferred Units required to be purchased by it at any such additional closing, then each Class A Preferred Unit held by such member would have automatically been converted into common units at the applicable adjustment ratio in effect with respect to such units immediately prior to such closing. All holders of Class A Preferred Units participated in additional closings at the required levels. Holders of Class B Preferred Units had the right and obligation to participate in additional closings of Class B Preferred Units upon the achievement of certain milestones by the Company. If any holder of Class B Preferred Units did not purchase the number of Class B Preferred Units required to be purchased by it at any such additional closing, then each Class B Preferred Unit held by such member would have automatically been converted into common units at the applicable adjustment ratio in effect with respect to such units immediately prior to such closing.

(vii) Initial Public Offering

In connection with preparation for an initial public offering, upon request of holder of at least 70% of the Preferred Units, all unit holders would have been required to have taken appropriate steps to implement a reorganization of the Company that may have included, for example, contribution of their units to a newly formed corporation.

(12) Equity-based Compensation and Equity Incentive Plans

Equity Plans

The Company has a number of equity plans, two of which are currently active.

The 2015 Equity Incentive Award Plan ("2015 Plan") was adopted by Mirna in 2015 and remains active after the Merger, now functioning as the primary equity plan for the Company. Following the Merger, there were 647,893 shares authorized under the 2015 Plan. The 2015 Plan includes an "evergreen provision" that allows for an annual increase in the number of shares of common stock available for issuance under the 2015 Plan, which annual increase will be added on the first day of each fiscal year from 2016 through 2025, inclusive, and will be equal to the lesser of (i) five percent of the shares outstanding on the last day of the immediately preceding fiscal year and (ii) such smaller number of shares as determined by the Board of Directors. The 2015 Plan provides for the granting of a variety of stock-based compensation awards, including stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, deferred stock awards, dividend equivalent awards, stock payment awards, performance awards and other stock-based awards.

The 2017 Stock Incentive Plan was adopted by Private Synlogic in 2017 at the time of the 2017 Reorganization and provides for the grant of incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and other stock-based awards. Under the 2017 Plan, 1,753,061 shares were initially authorized and reserved for issuance. Pursuant to the 2017 Reorganization, Private Synlogic issued restricted common stock awards under the 2017 Plan to replace the canceled incentive units pursuant to the termination of the 2015 LLC Plan ("2015 LLC Plan"). In addition, Private Synlogic also issued stock options to certain employees prior to the Merger. Pursuant to the Merger Agreement, each restricted common stock award of Private Synlogic under the 2017 Plan that was outstanding immediately prior to the Merger and each option to purchase common stock of Private Synlogic under the 2017 Plan that was outstanding and unexercised immediately prior to the Merger was converted into and became restricted

common stock and options to purchase shares of the Company's common stock, respectively, based on the Exchange Ratio of 0.5532 and the Company assumed the 2017 Plan.

The 2015 Employee Stock Purchase Plan ("ESPP") was adopted by Mirna in 2015 and allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their eligible compensation, subject to any plan limitations. The ESPP generally provides for set offering periods, and at the end of each offering period, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last trading day of the offering period. The Company suspended the ESPP in 2017.

The 2008 Long Term Incentive Plan ("2008 Plan") was adopted by Mirna in 2008 and allowed for the grant of incentive stock options to employees and nonqualified stock options and other equity awards to employees and nonemployees. The 2015 Plan is the successor to the 2008 Plan and at the time of the Merger, the remaining awards outstanding thereunder were cancelled and the number of shares with respect to those awards were transferred to the 2015 Plan. As of the Merger, the 2008 Plan was retired.

The 2015 LLC Plan was adopted by Private Synlogic at the time of the 2015 Reorganization, which provided for the grant of equity incentive units to employees, officers, directors or consultants. The 2015 LLC Plan was cancelled pursuant to the 2017 Reorganization as described above.

As of December 31, 2018, there were 477,414 shares available for future grant under the Company's two active equity incentive plans, the 2017 Plan and the 2015 Plan.

The Company is displaying all equity in its post-Merger amounts, as impacted by the Exchange Ratio.

Stock Options

The weighted average assumptions used in the Black-Scholes option-pricing model for stock options issued to employees under its two active equity plans, the 2015 Plan and the 2017 Plan, during the years ended December 31, 2018 and 2017 and to nonemployees during the year ended December 31, 2017 were:

	Year ended December 31,	
Employees:	**2018**	**2017**
Expected term	6.2 years	6.2 years
Weighted-average, risk-free interest rate	2.8%	2.1%
Expected volatility	70.8%	70.4%
Dividend yield	—	—

The following table summarizes stock option activity, as adjusted for the Exchange Ratio under the 2015 and 2017 Plans.

	Stock options outstanding			
	Number of options	**Weighted average exercise price**	**Weighted average remaining contractual term (in years)**	**Aggregate intrinsic value (a) (in thousands)**
Outstanding at December 31, 2017	1,267,221	$ 13.62	9.6	$ —
Granted	919,496	9.71		
Exercised	(19,830)	12.28		
Forfeited	(394,136)	12.09		
Expired	(32,867)	13.53		
Outstanding at December 31, 2018	1,739,884	11.92	9.0	$ —
Vested or expected to vest at December 31, 2018	1,739,884	11.92	9.0	$ —
Exercisable at December 31, 2018	489,236	13.20	8.4	$ —

(a) The aggregate intrinsic value is calculated as the difference between the exercise price of the options and the fair market value of the underlying common stock for the options that were in the money at December 31, 2018 . No options were in the money at December 31, 2018 .

During the years ended December 31, 2018 and 2017, 919,496 and 1,281,647 stock options were granted to employees and nonemployees, respectively. Approximately $3.2 million and $2.0 million in equity compensation was recognized related to stock options granted to employees and nonemployees for the years ended December 31, 2018 and 2017, respectively.

The weighted average grant date fair value per share of options granted to employees during the year ended December 31, 2018 was approximately $6.35. The total fair value of awards that vested during the year ended December 31, 2018 was $3.3 million.

As of December 31, 2018, there was approximately $8.4 million of unrecognized share-based compensation related to employees for unvested stock option grants which is expected to be recognized over a weighted average period of 2.6 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur. In addition, there was approximately $53,000 of unrecognized share-based compensation, related to unvested stock option grants to nonemployees which is expected to be recognized over a weighted average period of 2.4 years. The amount of equity-based compensation expense related to nonemployees that will ultimately be recorded will depend on the remeasurement of the outstanding awards through their vesting date.

Restricted Common Stock

During the year ended December 31, 2018, no shares of restricted common stock were granted. During the year ended December 31, 2017, 1,062,794 shares of restricted common stock were granted, including 1,059,912 shares of restricted common stock (adjusted for the Exchange Ratio) granted in exchange for the restricted common units and incentive units that were cancelled as part of the 2017 Reorganization. These shares retained the same vesting schedule as the cancelled restricted common units and incentive units. Private Synlogic treated these as modifications to the original grants of incentive units because the cancellation and reissuance was deemed to be concurrent. The calculation of the incremental compensation expense was based on the excess of the fair value of the award measured immediately before and after the modification. As a result of the modification, Private Synlogic recognized approximately $26,000 in equity-based compensation.

The following table shows restricted common stock activity:

	Restricted stock awards	
	Number of shares	Weighted average grant date fair value (per share)
Unvested at December 31, 2016	—	$ —
Awards exchanged upon 2017 Reorganization	1,059,912	13.53
Granted	2,884	19.01
Vested	(671,204)	13.54
Forfeited	(16,113)	13.53
Unvested at December 31, 2017	375,479	$ 13.55
Granted	—	—
Vested	(186,332)	13.54
Forfeited	(70,468)	13.61
Unvested at December 31, 2018	118,679	$ 13.54

During the years ended December 31, 2018 and 2017, 186,332 and 671,204 shares of restricted common stock vested and approximately $1.0 and $0.5 million in equity compensation was recognized, respectively.

As of December 31, 2018, there was approximately $0.2 million of unrecognized share-based compensation related to restricted stock awards granted to employees, which is expected to be recognized over a weighted average period of 1.6 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur. There was no unrecognized share-based compensation related to unvested restricted stock awards granted to nonemployees at December 31, 2018.

Incentive Units

Incentive units issued by Synlogic, LLC under the 2015 LLC Plan generally vested 25% after one year and ratably monthly thereafter over the next 36 months. Certain awards provided for accelerated vesting upon a change in control, as defined in the 2015 LLC Plan. Incentive units did not expire. Holders of incentive units had no voting rights in connection with such incentive units. Each incentive unit was intended to be a profits interest within the meaning of IRS regulations promulgated under the Internal Revenue Code. Each incentive unit had a threshold price, which was the price above which an incentive unit would participate in distributions. In this way, an incentive unit was designed to participate in the future profits and appreciation of Synlogic, LLC. Holders of incentive units would have been entitled to receive profits when and if distributions were in excess of the threshold price of the award set by the Board of Directors on the date of grant.

Synlogic, LLC measured and recorded the value of incentive units granted to nonemployees over the period of time that services were provided and, as such, unvested portions were subject to remeasurement at subsequent reporting periods.

No incentive units were issued during the years ended December 31, 2018 and 2017. In May 2017, all incentive units were cancelled pursuant to the 2017 Reorganization and reissued as restricted common stock. As a result, there was no incentive unit activity during the year ended December 31, 2018 or unrecognized compensation expense related to incentive units as of December 31, 2018

The following table represents a summary of incentive unit activity, as adjusted for the Merger, under the 2015 LLC Plan:

	Incentive units			
	Number of units	Weighted-average strike price	Weighted-average threshold price	Weighted-average grant date fair value
Non-vested units at December 31, 2016	971,906	$ 5.22	$ 5.93	$ 1.01
Granted	—	—	—	—
Vested	(73,719)	4.01	5.53	0.87
Forfeited	(260,145)	4.19	5.57	1.05
Non-vested units cancelled upon 2017 Reorganization	(638,042)	5.78	6.15	1.05
Non-vested units at December 31, 2017	—	$ —	$ —	$ —
Vested or expected to vest at December 31, 2017	—	$ —	$ —	$ —

Restricted Common Units

In May 2017, all restricted common unit awards were cancelled pursuant to the 2017 Reorganization and reissued as restricted common stock. As a result, there was no unrecognized compensation expense related to unvested restricted common units as of December 31, 2018.

The following table shows the restricted common unit activity for the year ended December 31, 2017, prior to the 2017 Reorganization, as adjusted for the Merger:

	Restricted common units	
	Number of units	Grant date fair value (per unit)
Unvested at December 31, 2016	219,087	$ 1.48
Granted	—	—
Vested	(37,770)	1.48
Forfeited	—	—
Exchanged as part of 2017 Reorganization	(181,317)	1.48
Unvested at December 31, 2017	—	$ —

Equity Compensation

The Company has recorded total equity-based compensation expense of approximately $4.3 million and $2.7 million, during the years ended December 31, 2018 and 2017, respectively. Equity compensation during the years ended December 31, 2018 and 2017 is derived from stock options and restricted stock awards. Equity-based compensation during the year ended December 31, 2018 also includes $0.7 million related to modifications in equity awards in connection with the separation of the Company's former Chief Executive Officer. Equity compensation during the year ended December 31, 2017 additionally includes equity compensation derived from incentive units and restricted common units granted prior to the 2017 Reorganization.

In July 2015, in connection with the 2015 Reorganization, all outstanding stock options and awards were canceled and reissued as incentive units and restricted common units. As such, equity compensation prior to the Merger was derived from incentive units and from a grant of restricted common units.

In May 2017, in connection with the 2017 Reorganization, the incentive units and restricted common units were cancelled and exchanged for restricted stock awards and stock options. Equity compensation after May 2017, was derived from stock options and restricted stock awards.

The following table summarizes equity-based compensation expense within the Company's consolidated statements of operations and comprehensive loss for the years ended December 31, 2018 and 2017 (in thousands):

	Years ended December 31,	
	2018	2017
Research and development	$ 1,333	$ 1,410
General and administrative	2,984	1,242
	$ 4,317	$ 2,652

The following table summarizes equity-based compensation expense by type of award for the years ended December 31, 2018 and 2017 (in thousands):

	Years ended December 31,	
	2018	2017
Stock options	$ 3,361	$ 1,956
Restricted stock awards	956	508
Incentive units	—	132
Restricted common units	—	56
	$ 4,317	$ 2,652

(13) Distributions

The Board of Directors of Synlogic, LLC had the authority to determine the amount, if any, of proceeds available for distribution to unit holders. In the event that a distribution of proceeds was declared by the Board of Directors, such proceeds would have been distributed in accordance with the following order of priority:

- first, to holders of Class B Preferred Units, pro rata in proportion to their unpaid contributed capital, until such holder had received an amount equal to its capital contribution;
- second, to holders of Class A Preferred Units and Class A Contingently Redeemable Preferred Units, pro rata in proportion to their unpaid contributed capital, until such holder had received an amount equal to its capital contribution;
- third, to all holders of preferred units, common units and incentive units, pro rata in proportion to the remaining amount to be distributed, until an aggregate amount had been distributed in respect of each preferred unit, common unit and incentive unit equal to the greatest aggregate amount per unit distributed in respect of any preferred unit under the first and second priority described above; provided, that no holder of an incentive unit shall participate in any distributions until a total amount equal to the threshold price with respect to such incentive unit has been distributed in respect of any common unit outstanding on the date of issuance of such incentive unit subsequent to the issuance of such incentive unit;

- fourth, to each holder of certain incentive units for which the Board of Directors had established a strike price, pro rata in proportion to the remaining amount to be distributed, an amount equal to the difference between the strike price for such incentive unit, and the threshold price for such incentive unit; and
- thereafter, to all holders of preferred units, common units and incentive units, pro rata in proportion to their percentage interest.

No distributions were made to unit holders prior to the 2017 Reorganization.

(14) Significant Agreements

AbbVie Collaboration Agreement

In July 2015, the Company entered into the AbbVie Agreement under which the Company granted AbbVie an exclusive option to purchase IBDCo and, in exchange, agreed to collaborate in researching and developing an Investigational New Drug ("IND") candidate for the treatment of IBD. The AbbVie Agreement sets forth the Company's and AbbVie's respective obligations for development and delivery of an IND candidate package using reasonable commercial efforts.

In exchange for the exclusive option to acquire IBDCo, initial research and development services for drug discovery and pre-clinical development, and participation on the joint research committee ("JRC"), AbbVie agreed to pay IBDCo an upfront, nonrefundable cash payment of $2.0 million, which IBDCo received in December 2015. AbbVie also agreed to pay IBDCo up to $16.5 million in milestone payments associated with specified research and pre-clinical events, which were determined to represent customer options for accounting purposes, as well as an option exercise fee upon the execution of their option to buy IBDCo and other royalty and milestone payments. The upfront cash payment and any payments for option fees and royalties are non-refundable, non-creditable and not subject to set-off.

The research and development will be performed by the Company over four phases of research defined in the research plan. The Company is eligible to receive payments from AbbVie upon the election to continue the research and development at the achievement of certain milestone events. The JRC will make a determination as to the continuation of the collaboration at the achievement of research and pre-clinical milestones, except for the final milestone, which AbbVie has the discretion to determine achievement without the approval of the JRC. If the parties make the determination to continue on with the AbbVie Agreement upon achievement of each milestone event, then AbbVie will pay the consideration associated with that milestone and the collaboration will continue through the remaining term of the option to purchase IBDCo, which was initially considered to be approximately 54 months. However, AbbVie has the right to terminate the contract at any time with 90 days' notice.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, AbbVie, is a customer. The Company identified the following material promises at the outset of the arrangement: (1) a non-exclusive royalty-free research and development license; (2) research and development services for pre-clinical activities under the research plan through to the first research and development phase (or an estimated 17 months); (3) three option rights for AbbVie to continue the collaboration as related to three phases of research and development; (4) participation on the JRC; and (5) the transfer of ownership of IBDCo upon exercise of the option to buy IBDCo. The Company determined that the license and research and development activities were not distinct from one another. Participation on the JRC to oversee the research and development activities was determined to be quantitatively and qualitatively immaterial and therefore is excluded from performance obligations. As such, the Company determined that the license and research and development services should be combined into a single performance obligation.

The Company evaluated the milestone payments, which represent customer options as described above, and the option to purchase IBDCo, to determine whether they provide AbbVie with any material rights. The Company concluded that the options were not issued at a significant and incremental discount, and therefore do not provide material rights. As such, they were excluded as performance obligations at the outset of the arrangement. If AbbVie elects to exercise the options, the additional consideration will be added to the transaction price and allocated to the resulting performance obligations.

Based on these assessments, the Company identified one performance obligation at the outset of the AbbVie Agreement, which consists of: (1) the non-exclusive license and (2) the research and development activities through the first research and development phase.

At the outset of the arrangement, the transaction price included only the $2.0 million up-front consideration received which was allocated to the single performance obligation. The option exercise fees ($16.5 million for the milestones and the IBDCo purchase option exercise fee) that may be received are excluded from the transaction price until each customer option is exercised. The

Company reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

In May 2017, the Company completed the research and development services for the first phase of the research plan and was paid $2.0 million to commence the second phase of the research plan. At this time, the $2.0 million was added to the transaction price and allocated to a new performance obligation consisting of the underlying license and research and development services to be performed over the second phase of the research plan.

On September 27, 2018, AbbVie and the Company signed an amendment (the "Amendment") to the AbbVie Agreement. The Amendment clarified the requirements necessary to complete the second phase which resulted in additional time and effort in the second phase of the research plan. Additionally, the Amendment split the next milestone payment under the AbbVie Agreement into two payments: a milestone payment of $2.0 million earned by the Company upon execution of the Amendment and the remaining milestone payment of the balance due upon the successful achievement of specified research and pre-clinical events and the advancement to the third phase of the research plan.

The Company determined that the Amendment represented a modification to the AbbVie Agreement. The additional research and development services are not distinct from the remaining research and development services under the second phase of the research plan of the AbbVie Agreement. The Amendment was accounted for as part of the original AbbVie Agreement and the services form part of the single performance obligation that was partially satisfied as of the date of the contract modification. As a result, the transaction price for the current performance obligation associated with the second phase of the research plan increased by $2.0 million. The impact of the contract modification on the transaction price and the measure of progress toward completion of the performance obligation was recognized as an adjustment to revenue upon execution of the Amendment on a cumulative catch-up basis. The cumulative catch-up adjustment to revenue, as a result of the contract modification, was $1.8 million recognized during September 2018. Additionally, deferred revenue increased by $0.3 million as a result of the contract modification.

Revenue associated with performance obligations under the AbbVie Agreement are recognized as the research and development services are provided using an input method, according to the full time equivalents incurred. The research and development activities are expected to be performed over a period of approximately 54 months. The transfer of control occurs over time and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The amounts received that have not yet been recognized as revenue are recorded in deferred revenue on the Company's consolidated balance sheet.

For the years ended December 31, 2018 and 2017, the Company had recognized $ 2.5 million and $2.4 million, respectively, as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss. Deferred revenue amounted to $0.3 million as of December 31, 2018, all of which is included in current liabilities.

License Agreement with the Massachusetts Institute of Technology and Boston University

In April 2017, the Company exercised an option associated with the October 2014 agreement with Boston University and the Massachusetts Institute of Technology to acquire a license for certain intellectual property in exchange for $50,000. The execution of this option triggered an equity award for the issuance of 325,377 common units, which were converted to 325,377 common shares upon the 2017 Reorganization and converted to 179,999 common shares during the Merger. Based on the fair value of common units at the time of the execution of the license, the Company recognized license fees of approximately $1.8 million upon issuance of the common units associated with the equity award. Additionally, the Company was required to pay approximately $0.3 million for prior patent costs incurred in connection with the option agreement. The Company recorded these amounts, including the fair value of the common stock issued to the licensors as research and development expense in the 2017 consolidated statement of operations, as the licenses do not have future alternative use, in accordance with ASC Topic 730, *Research and Development.*

The Company determined that its growing portfolio of internally generated intellectual property superseded the in-licensed intellectual property in the BU license and the MIT license. Accordingly, on December 18, 2018, it provided notice to terminate the license agreements with MIT and BU/MIT. The BU license will be terminated effective as of February 16, 2019 and the MIT license will be terminated effective as of June 19, 2019.

Sales Agreement with Cowen and Company

On October 13, 2017 the Company entered into a sales agreement with Cowen and Company, LLC ("Cowen") with respect to an at-the-market ("ATM") offering program under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock through Cowen as its sales agent. In an ATM offering, exchange-listed companies incrementally sell

newly issued shares into the secondary trading market through a designated broker-dealer at prevailing market prices. No sales of common stock were made pursuant to the ATM during 2017 and 2018.

(15) Net Loss per Share

The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders (in thousands, except for share and per share amounts):

	2018	2017
Numerator:		
Net loss attributable to common stockholders	$ (48,435)	$ (40,377)
Denominator:		
Weighted-average common shares outstanding - basic and diluted	23,882,685	6,724,641
Net loss per share attributable to common stockholders - basic and diluted	$ (2.03)	$ (6.00)

The Company's potentially dilutive shares, which include outstanding stock options and unvested restricted common stock, are considered to be common share equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following potential common shares, presented based on amounts outstanding at each period end, were excluded from the calculation of the diluted net loss per share attributable to common stockholders for the period indicated because including them would have had an anti-dilutive effect.

	As of December 31,	
	2018	2017
Unvested restricted common stock awards	118,679	375,479
Outstanding options to purchase common stock	1,739,884	1,267,221

(16) Income Taxes

The provision for income taxes consist of the following (in thousands):

	December 31,	
	2018	2017
Current Tax Expense:		
Federal	$ —	$ —
State	33	—
	$ 33	$ —

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. Deferred tax assets consist of the following (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 33,275	$ 21,248
Tax credit carryforwards	4,365	3,038
Accrued expenses	103	32
Property and equipment	—	390
Deferred rent	2,209	53
Equity compensation	784	503
Amortizable intangibles	1,339	1,492
Other	78	—
Gross deferred tax assets	42,153	26,756
Deferred tax liability:		
Other	—	(241)
Property and equipment	(1,863)	—
Valuation allowance	(40,290)	(26,515)
Net deferred tax assets	$ —	$ —

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of the Company's deferred tax assets, which are comprised principally of net operating loss carryforwards, and determined that it is more likely than not that the Company will not recognize the benefits of the deferred tax assets. As a result, a full valuation allowance of approximately $40.3 million and $26.5 million was established at December 31, 2018 and 2017, respectively.

A reconciliation of the statutory federal income tax rate to the Company's effective income tax rate is as follows (dollars in thousands):

	Years ended December 31,	
	2018	2017
	Tax Rate	Tax Rate
U.S. federal statutory rate	21%	34%
State income taxes, net of federal benefit	6%	5%
Other permanent differences	(1)%	(1)%
Tax credits	3%	5%
Other items	(1)%	—
Change in rate due to Tax Reform	—	(27)%
Mirna acquisition	—	17%
Net change in valuation allowance	(28)%	(33)%
Effective income tax rate	—	—

A roll-forward of the valuation allowance for the years ended December 31, 2018 and 2017 is as follows (in thousands):

	Years ended December 31,	
	2018	2017
Balance at beginning of year	$ (26,515)	$ (13,060)
Increase in valuation allowance	(13,775)	(13,455)
Balance at end of year	$ (40,290)	$ (26,515)

As of December 31, 2018 and 2017, the Company had federal and state net operating loss carryforwards that may be available to reduce future taxable income of approximately $125.5 million and $82.0 million, respectively, which begin to expire in 2034. In addition, at December 31, 2018, the Company had federal and state research and development tax credit carryforwards available to reduce future tax liabilities of approximately $2.8 million and $1.6 million, respectively. These credits begin to expire in 2034 and 2029, respectively.

Pursuant to Section 382 of the Internal Revenue Code of 1986 (“IRC”), certain substantial changes in the Company’s ownership may result in a limitation on the amount of net operating loss (“NOL”) carryforwards and research and development credit (“R&D credit”) carryforwards that may be used in future years. Utilization of the NOL and R&D credit carryforwards may be subject to a substantial annual limitation under Section 382 of the IRC due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has not completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since its formation, due to a significant complexity and related costs associated with such a study. There could be additional ownership changes in the future that may result in additional limitations on the utilization of NOL carryforwards and credits.

The Company is required to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. The Company has not recognized any liability for unrecognized tax benefits as of December 31, 2018.

The Company files tax returns, on an entity-level basis, as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. Tax years from 2015 to the present are open to examination under the statute. The Company’s policy is to record interest and penalties related to income taxes as part of the tax provision. There are no interest or penalties accrued at December 31, 2018 and 2017.

Effects of the Tax Cuts and Jobs Act

On December 22, 2017, President Trump signed into U.S. law the Tax Cuts and Jobs Act of 2017 (“Tax Reform”). ASC Topic 740, *Accounting for Income Taxes*, requires companies to recognize the effect of tax law changes in the period of enactment even though the effective date for most provisions is for tax years beginning after December 31, 2017, or in the case of certain other provisions of the law, January 1, 2018. Given the significance of the legislation, the U.S. Securities and Exchange Commission (the "SEC") staff issued Staff Accounting Bulletin ("SAB") No. 118 (“SAB 118”), which allows registrants to record provisional amounts during a one year “measurement period” similar to that used when accounting for business combinations. However, the measurement period is deemed to have ended earlier when the registrant has obtained, prepared, and analyzed the information necessary to finalize its accounting. During the measurement period, impacts of the law are expected to be recorded at the time a reasonable estimate for all or a portion of the effects can be made, and provisional amounts can be recognized and adjusted as information becomes available, prepared, or analyzed.

SAB 118 summarizes a three-step process to be applied at each reporting period to account for and qualitatively disclose: (1) the effects of the change in tax law for which accounting is complete; (2) provisional amounts (or adjustments to provisional amounts) for the effects of the tax law where accounting is not complete, but that a reasonable estimate has been determined; and (3) a reasonable estimate cannot yet be made and therefore taxes are reflected in accordance with law prior to the enactment of the Tax Cuts and Jobs Act.

However, several provisions of the Tax Reform have significant impact on the Company’s U.S. tax attributes, generally consisting of credits, loss carry-forwards, and amortizable intangibles. The provisional reporting period ended on December 22, 2018. The Company has reevaluated its assets and liabilities associated with such future tax benefits in the current year and determined that no further adjustment is necessary to its deferred tax asset and liabilities. This reduction in the deferred tax asset has been offset by a coinciding reduction in the associated valuation allowance, creating a zero net impact to the Company’s statement of operations. The Company’s tax attributes are generally subject to a full valuation allowance in the United States and thus, any adjustments to the attributes will not impact the tax provision. Although the Company has made a reasonable estimate of the gross amounts of the attributes disclosed, a final determination of the Tax Reform’s impact on the attributes and related valuation allowance requirements remain incomplete pending a full analysis of the provisions and their interpretations.

Other significant provisions that are not yet effective but may impact income taxes in future years include: a limitation on the current deductibility of net interest expense in excess of 30 percent of adjusted taxable income and a limitation of net operating losses generated after fiscal 2018 to 80 percent of taxable income.

(17) Leases

The Company recorded rent expense of approximately $2.5 million for the year ended December 31, 2018. The Company recorded a rent credit of approximately $0.2 million for the year ended December 31, 2017 due to the accelerated amortization the deferred rent associated with the 200 Sidney Street facility. In July 2017, the Company agreed to terminate its lease and revised its estimate of the remaining amortization period from 63 months to seven months.

Operating Leases

In July 2017, the Company entered into an agreement to lease approximately 41,346 square feet of laboratory and office space at 301 Binney Street in Cambridge, Massachusetts. Annual rent is approximately $3.1 million. The ten-year lease commenced in January 2018 and contains provisions for a free-rent period, annual rent increases and an allowance for tenant improvements. The Company is responsible for real estate taxes, maintenance, and other operating expenses applicable to the leased premises. In addition to approximately $1.6 million the Company has committed to for tenant improvements, the operating lease also provided for a tenant improvement allowance, at the cost of the lessor, not to exceed approximately $6.6 million. The Company was deemed to be the accounting owner of the tenant improvements primarily because it was responsible for project cost overruns. Therefore, the amounts will be recorded as a leasehold improvement and deferred rent and will be recorded as a reduction to rent expense ratably over the lease term. At December 31, 2018, the Company has capitalized approximately $5.0 million of the landlord-funded tenant improvements, representing the completed portion of the buildout. In conjunction with the lease, the Company established a letter of credit of approximately $1.0 million secured by cash balances included in restricted cash.

In July 2015, the Company entered into an operating lease for office and laboratory space at 200 Sidney Street in Cambridge, Massachusetts. The operating lease term commenced in February 2016 and expired in April 2021 with a one year renewal option to extend the lease. The Company agreed to terminate the lease in July 2017 at a date that was 30 days after the commencement of its new lease. No penalties were associated with the termination of the lease. Rent expense commenced on February 1, 2016 and was recognized on a straight-line basis over the duration of the term. The operating lease provided for annual rent of approximately $0.9 million, payable on a monthly basis, which increased at a rate of 3% annually, and included three months of rent abatement during the first year. The Company was responsible for real estate taxes, maintenance, and other operating expenses applicable to the leased premises. The Company was deemed to be the accounting owner of the tenant improvements primarily because it was responsible for project cost overruns. Therefore, the amounts were recorded as a leasehold improvement and deferred rent and were being recorded as a reduction to rent expense ratably over the lease term of 63 months. As a result of the agreement to terminate its lease, the Company revised its estimate of the remaining amortization period of the deferred rent and its estimate of the remaining useful life of its leasehold improvements to seven months through January 2018.

Capital Leases

In June 2017, the Company entered two non-cancellable thirty-six month lease agreements for certain lab equipment of approximately $0.2 million and $0.7 million, respectively. The lease term and payments for each agreement began upon delivery and installation of the equipment. Both leases are accounted for as a capital lease as one has a bargain purchase option and in the other, the present value of the lease exceeds 90% of the fair market value. At December 31, 2018, the interest rate on each capital lease obligation was approximately 1.1% and 7.3%, respectively.

In October 2016, the Company entered into a twenty-four month, non-cancellable lease agreement for approximately $0.4 million for certain lab equipment. Due to the existence of a bargain purchase option, the lease has been accounted for as a capital lease. At December 31, 2017, the interest rate on the outstanding capital lease obligation was approximately 9.6%. The agreement terminated per the terms of the lease agreement in November 2018.

Future minimum lease payments under the Company's non-cancelable operating and capital leases as of December 31, 2018, are as follows (in thousands):

	Operating leases	Capital leases
Fiscal year:		
2019	$ 3,175	$ 287
2020	3,270	214
2021	3,369	2
2022	3,470	—
2023	3,574	—
Thereafter	18,067	—
Total future minimum lease payments	$ 34,925	$ 503
Less amounts representing interest		27
Capital lease obligations at December 31, 2018		476
Less current portion of capital lease obligations		266
Capital lease obligations, net of current portion		$ 210

(18) Commitments and Contingencies

On December 7, 2018, Synlogic Operating Company, Inc., a wholly-owned subsidiary of Synlogic, Inc. (the "Company"), entered into a Statement of Work (the "SOW") with Azzur Group, LLC ("Azzur") pursuant to a Master Contract Services Agreement (the "Master Services Agreement"), dated September 8, 2018, between the Company and Azzur.

Pursuant to the SOW, Azzur has agreed to provide the Company with access to, and the use of, an approximately 700 square foot cleanroom space to be constructed in Waltham, Massachusetts (the "Azzur Suite"), for a period of 44 months, from May 1, 2019 to December 31, 2022 (the "Term"). Azzur has also agreed to provide the Company with storage space and personnel support at the Azzur Suite. The total estimated project cost during the Term for access to, and use of, the cleanroom and storage space, and the personnel support and other services, is $4.8 million.

The Company may terminate the SOW on four months' prior written notice at any time during the Term. In addition, either party may terminate the Master Services Agreement (including the SOW) due to a breach by the other party and failure to cure. If the Azzur Suite is not ready for use by the Company as of May 1, 2019, the Company may (i) elect to terminate the SOW, (ii) wait for the Azzur Suite to become available, without incurring any costs (other than a deposit) relating to the Azzur Suite until it becomes available, or (iii) accept an alternate cleanroom space from Azzur on different terms.

In the ordinary course of business, the Company may be subject to legal proceedings, claims and litigation as the Company operates in an industry susceptible to patent legal claims. The Company accounts for estimated losses with respect to legal proceedings and claims when such losses are probable and estimable. Legal costs associated with these matters are expensed when incurred. The Company is not currently a party to any material legal proceedings.

(19) Employee Benefits

The Company has a defined contribution 401(k) plan for eligible employees. Employees are eligible to participate in the plan beginning on their date of hire. Under the terms of the plan, employees may make voluntary contributions as a percentage of compensation. The Company has not made any matching contributions since the adoption of the 401(k) plan.

(20) Related-Party Transactions

During the year ended December 31, 2018, there were no related-party transactions. During the year ended December 31, 2017, before the Company became a public company, the Company received repayment of the loan to its then-existing chief executive officer of approximately $0.2 million. The loan was repaid in June 2017, including interest which accrued at a rate of 0.6%.

(21) Selected Quarterly Data (Unaudited)

The following tables contain quarterly financial information for 2018 and 2017 (in thousands). The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2018 Quarter Ended			
	March 31	June 30	September 30	December 31
Revenue	$ 354	$ 254	$ 1,801	$ 111
Operating expenses	11,990	15,606	13,335	$ 12,819
Loss from operations	(11,636)	(15,352)	(11,534)	$ (12,708)
Net loss	(11,165)	(14,591)	(10,748)	$ (11,931)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.55)	$ (0.59)	$ (0.43)	$ (0.47)

	2017 Quarter Ended			
	March 31	June 30	September 30	December 31
Revenue	$ 111	$ 2,111	$ 111	$ 111
Operating expenses	7,485	11,568	12,186	12,029
Loss from operations	(7,374)	(9,457)	(12,075)	(11,918)
Net loss	(7,368)	(9,388)	(11,924)	(11,697)
Net loss per share attributable to common stockholders - basic and diluted	$ —	$ (4.70)	$ (1.66)	$ (0.74)
Net loss per unit attributable to common unit holders - basic and diluted	$ (4.49)	$ —	$ —	$ —

(22) Subsequent Events

On February 28, 2019, the Joint Research Committee related to the Company's collaboration with AbbVie concluded that the remaining milestone of $2.5 million under the Second Amendment in the Company's collaboration with AbbVie was achieved. Related revenue will be recognized as the research and development services are provided using an input method, according to the full time equivalents incurred over the third phase of the research plan.

Exhibit 10.25

THIRD AMENDMENT TO AGREEMENT AND PLAN OF MERGER
FIRST AMENDMENT TO LICENSE AGREEMENT

This **THIRD AMENDMENT TO AGREEMENT AND PLAN OF MERGER and FIRST AMENDMENT TO LICENSE AGREEMENT** (this "**Third Amendment**"), is entered into as of December [18], 2018 (the "**Third Amendment Effective Date**"), by and among AbbVie S.A.r.l., a corporation organized under the laws of Luxembourg ("**Buyer**"), Synlogic IBDCo, Inc., a Delaware corporation (the "**Company**") and Synlogic Operating Company, Inc., a Delaware corporation formerly known as, and as successor to, Synlogic, LLC (the "**Parent**").

RECITALS

WHEREAS, Buyer, Company, Parent, Suffolk Merger Sub, Inc., a Delaware corporation ("**Merger Sub**"), Synlogic, Inc., a wholly-owned subsidiary of the Parent ("**Synlogic**"), and certain individuals (the "**Founders**") (each of the Founders, Buyer, Merger Sub, Company, Parent and Synlogic are sometimes referred to herein individually as a "**Party**," and collectively as the "**Parties**"), entered into an Agreement and Plan of Merger, dated as of July 16, 2015 (as amended, the "**Merger Agreement**"; capitalized terms not otherwise defined herein shall the respective meanings assigned to such terms in the Merger Agreement);

WHEREAS, Parent and Company entered into a License Agreement dated as of July 16, 2015 (as amended, the "**License Agreement**");

WHEREAS, Buyer, Parent and the Company first amended the Merger Agreement pursuant to that certain First Amendment to Agreement and Plan of Merger dated as of December 14, 2015;

WHEREAS, Buyer, Parent and the Company also amended the Merger Agreement pursuant to that certain Second Amendment to Agreement and Plan of Merger dated as of September 27, 2018;

WHEREAS, pursuant to Section 12.6(c) of the Merger Agreement, the Merger Agreement may be amended by Buyer, Parent and the Company;

WHEREAS, pursuant to Section 9.9 of the License Agreement, the License Agreement may be amended by Buyer, Parent and the Company; and

WHEREAS, Buyer has provided its written consent to Parent's termination of the University Licenses and, in connection therewith, the Parties desire to further amend the Merger Agreement and to amend the License Agreement as set forth herein.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants and conditions contained in this Third Amendment, the Parties agree as follows:

Portions of this Exhibit, indicated by the mark "[***]", were omitted and have been filed separately with the Secretary of the Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

1. Amendments to ARTICLE I of the Merger Agreement

   a. The definition of "[***]" set forth in Section 1.13 of the Merger Agreement is hereby deleted in its entirety and replaced with "1.13 [*Intentionally Omitted*]".

   b. The definition of "[***]" set forth in Section 1.139 of the Merger Agreement is hereby deleted in its entirety and replaced with "1.139 [*Intentionally Omitted*]".

   c. The definition of "University Licenses" set forth in Section 1.214 of the Merger Agreement is hereby deleted in its entirety and replaced with the following new Sections and definitions in the appropriate alphabetical order:

      "Section 1.214 "*University Party*" means either [***], their respective Affiliates or any combination thereof.

      Section 1.214A "*University Patent Right"* means any Patent Right that (i) was, or absent termination would have been, the subject of the [***] among [***] or (ii) was, or absent termination would have been, the subject of the [***] between [***]."

2. Amendment to Section 2.10(c)(ii) of the Merger Agreement.

   Section 2.10(c)(ii) of the Merger Agreement is hereby amended by inserting the following sentence at the end thereof:

   "Notwithstanding the foregoing and the last sentence of Section 2.10(c)(iii), in the event that, after the Closing Date, Buyer determines that it is necessary to enter into an agreement negotiated on arms' length terms with [***] in order to obtain a license under any [***] owned or controlled by [***] in a particular country or other jurisdiction which, but for such license, would be infringed by the manufacture, use or sale of such Product in such country or other jurisdiction, Buyer shall be entitled to deduct [***] actually paid to [***] from [***] that would otherwise be owed under this Section 2.10(c) with respect to [***] in the applicable country or other jurisdiction."

3. Amendments to ARTICLE I of the License Agreement

   a. The definition of "[***]" set forth in Section 1.7 of the License Agreement is hereby deleted in its entirety and replaced with "1.7 [*Intentionally Omitted*]".

   b. The definition of "[***]" set forth in Section 1.36 of the License Agreement is hereby deleted in its entirety and replaced with "1.36 [*Intentionally Omitted*]".

4. General Amendment to Merger Agreement.

   a. The Merger Agreement is further amended by deleting all references to the "University Licenses", the "[***]" and the "[***]", including any and all terms and conditions in the Merger Agreement pertaining to the such references (including without limitation such references to the University Licenses, [***] and/or [***], as the case may be, in Sections 4.2(h), 5.13(q), 5.13(r), 7.1(b)(xiv) and 7.15 of the Merger Agreement.

   b. For avoidance of doubt, the terms and conditions of the Merger Agreement shall, unless the context expressly requires otherwise, shall be interpreted to account for the termination of the University Licenses.

5. General Amendment to License Agreement.

   a. The License Agreement is further amended by deleting all references to the "[***]" and the "[***]", including any and all terms and conditions in the License Agreement pertaining to such references (including without limitation Sections 2.5, 2.6 and 6.2 of the License Agreement).

   b. For avoidance of doubt, the terms and conditions of the License Agreement shall, unless the context expressly requires otherwise, shall be interpreted to account for the termination of the [***] and the [***].

5. Jurisdiction. This Third Amendment was prepared in the English language, which language shall govern the interpretation of, and any dispute regarding, the terms of this Third Amendment. This Third Amendment and all disputes arising out of or related to this Third Amendment or any breach hereof shall be governed by and construed under the laws of the State of Delaware, USA, without giving effect to any choice of law principles that would require the application of the laws of a different jurisdiction.

6. Certain Conflicts. Where there is any conflict between the terms of this Third Amendment and the terms of the Merger Agreement, the License Agreement or any other agreement between the Parties (or their respective Affiliates), the terms of this Third Amendment shall prevail.

7. Effect of Amendment. Except as expressly set forth in this Third Amendment, all other terms of the Merger Agreement and the License Agreement shall apply and remain in full force and effect.

8. Counterparts. This Third Amendment may be executed in one (1) or more counterparts, by original, facsimile or PDF signature, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Signatures to this Third Amendment transmitted by facsimile, by email in "portable document format" (".pdf"), or by any other electronic means intended to preserve the original graphic and pictorial appearance of this Agreement shall have the same effect as physical delivery of the paper document bearing original signature.

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IN WITNESS WHEREOF, the Parties have executed this Third Amendment by their duly authorized officers as of the Third Amendment Effective Date.

ABBVIE S.À.R.L.

By: */s/ Sophie Morlet*
Name: Sophie Morlet
Title: Category A Manager

SYNLOGIC OPERATING COMPANY, INC.

By: */s/ Aoife Brennan*
Name: Aoife Brennan
Title: President and CEO

SYNLOGIC IBDCo, INC.

By: */s/ Aoife Brennan*
Name: Aoife Brennan
Title: President and CEO

Portions of this Exhibit, indicated by the mark "[***]", were omitted and have been filed separately with the Secretary of the Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.29

MASTER CONTRACT SERVICES AGREEMENT

THIS MASTER CONTRACT SERVICES AGREEMENT (together with Appendix A and any Statement(s) of Work (as defined in Section 1), the **"Agreement"**) is made on 08 September, 2018 (the "Effective Date") by and between Synlogic Operating Company, Inc., having offices at 301 Binney Street, Suite 402, Cambridge, MA 02142 ("Synlogic") and Azzur Group (d/b/a Azzur of New England LLC), a Pennsylvania Limited Liability Company with an office at 411 Waverley Oaks Rd., #126, Waltham MA 02452 **("Service Provider"**).

1. Agreement Structure. From time to time, Synlogic may want Service Provider to provide certain services **("Services"**). This Agreement contains general terms and conditions under which Synlogic would engage Service Provider and under which Service Provider would provide Services. Synlogic and Service Provider must complete and execute a work order, project order or statement of work referencing this Agreement (each, a **"Statement of Work"**) before any Services are provided. Each Statement of Work will include, at a minimum, the information relating to the specific Services outlined in the sample Statement of Work attached as Appendix A. Neither Synlogic nor Service Provider is obligated to execute any Statement of Work. Once executed, each Statement of Work becomes part of this Agreement, although the terms in a Statement of Work will apply only to Services described in that Statement of Work. A Statement of Work may not change any term in this Agreement.

2. About Services.

2.1 Provision of Services. Service Provider agrees to provide all Services identified in any Statement of Work: (a) within the time period specified in the relevant Statement of Work; and (b) in accordance with the highest prevailing industry standards and practices for the performance of similar services. For each Statement of Work, Service Provider will designate a **"Project Leader"** who will be available for frequent communications with Synlogic regarding Services provided under that Statement of Work, as well as contacts for administrative and payment matters for those Services. Synlogic will designate a **"Synlogic Representative"** who will be the point of contact for the Project Leader.

2.2 Change Orders. If either party identifies a need to modify a Statement of Work, the identifying party will notify the other party in writing as soon as reasonably possible. Service Provider will use reasonable efforts to provide to Synlogic within [***] after receiving or providing the notice described above a written change order containing a description of the required modifications and their effect on the scope, fees and timelines specified in the Statement of Work (each, a **"Change Order"**). No Change Order will be effective unless and until it has been signed by an authorized representative of each party. If Synlogic does not approve a Change Order and has not terminated the Statement of Work, but still desires that the Statement of Work be modified, then the parties will use reasonable good faith efforts to agree on a Change Order that is mutually acceptable. Service Provider will continue to work under the existing Statement of Work during any such negotiations, to the extent such efforts are practicable and would facilitate the completion of the work envisioned in the Statement of Work, but will not commence work in accordance with the Change Order until it is authorized in writing by Synlogic.

2.3 Subcontracting. With Synlogic's prior written consent, Service Provider may subcontract the performance of specific obligations of Service Provider under a Statement of Work to an Affiliate (as defined below in this Section 2.3) of Service Provider or to a qualified non-Affiliate third party including consultants; *provided,* that (a) such Affiliate or third party performs those Services in a manner consistent with the terms and conditions of this Agreement; and (b) Service Provider remains liable for the performance of such Affiliate or third party. **"Affiliate"** means, with respect to either Synlogic or Service Provider, any corporation, company, partnership, joint venture and/or firm which controls, is controlled by or is under common control with Synlogic or Service Provider, as applicable. As used in this Section 2.3, **"control"** means (i) in the case of corporate entities, direct or indirect ownership of more than fifty percent (50%) of the stock or shares having the right to vote for the election of directors (or such lesser percentage that is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction); and (ii) in the case of non-corporate entities, the direct or indirect power to manage, direct or cause the direction of the management and policies of the non-corporate entity or the power to elect more than fifty percent (50%) of the members of the governing body of such non-corporate entity.

2.4 Regulatory Contacts. Synlogic will be solely responsible for all contacts and communications (including submissions of information) with any regulatory authorities with respect to matters relating to Services. Unless required by applicable law, Service Provider will have no contact or communication with any regulatory authority regarding Services without the prior written consent of Synlogic, which consent will not be unreasonably withheld. Service Provider will notify Synlogic promptly, and in no event later than one (1) business day, after Service Provider receives any contact or communication from any regulatory authority relating in any way to Services and will provide Synlogic with a summary of such contact and copies of any such communication within one (1) business day after Service Provider's receipt of such contact or communication. Unless prohibited by applicable law, Service Provider will consult with Synlogic regarding the response to any inquiry or observation from any regulatory authority relating in any way to Services and will allow Synlogic at its discretion to control and/or participate in any further contacts or communications relating to Services. Service Provider will comply with all reasonable requests and comments by Synlogic with respect to all contacts and communications with any regulatory authority relating in any way to Services.

2.5 Key Service Provider Personnel. All Service Provider Personnel (as defined in Section 3.4) identified in a Statement of Work as **"Key Service Provider Personnel"** will remain assigned to perform Services covered by the applicable Statement of Work as long as such individuals remain employed by or under contract with Service Provider, unless (a) an individual is unavailable for reasons of disability, illness or promotion; or (b) Synlogic has requested the replacement of any individual who is not performing to Synlogic's reasonable satisfaction. Service Provider will cooperate with Synlogic in periodically reviewing the performance of the Key Service Provider Personnel and will promptly remedy any concerns to Synlogic's reasonable satisfaction. Service Provider will promptly select a qualified replacement should any Key Service Provider Personnel resign or become otherwise unavailable as specified above or if Synlogic requests the replacement of any such Key Service Provider Personnel. Synlogic will have the right to approve any such replacement, which approval will not be unreasonably withheld.

3. Representations and Warranties of Service Provider. Service Provider represents and warrants as follows:

3.1 Organization of Service Provider. Service Provider is and will remain a corporation or company duly organized, validly existing and in good standing under the laws of its jurisdiction of organization.

3.2 Enforceability of this Agreement. The execution and delivery of this Agreement by Service Provider has been authorized by all requisite corporate or company action. This Agreement is and will remain a valid and binding obligation of Service Provider, enforceable in accordance with its terms, subject to laws of general application relating to bankruptcy, insolvency and the relief of debtors.

3.3 Absence of Other Contractual Restrictions. Service Provider is under no contractual or other obligation or restriction that is inconsistent with Service Provider's execution or performance of this Agreement. Service Provider will not enter into any agreement, either written or oral, that would conflict with Service Provider's responsibilities under this Agreement.

3.4 Qualifications of Service Provider Personnel. Service Provider has engaged, will engage and will cause its Affiliates involved in rendering Services to engage, employees and permitted subcontractors including consultants (collectively, **"Service Provider Personnel"**) with the proper skill, training, availability and experience to provide Services. Before providing Services, all Service Provider Personnel must be subject to binding written agreements with Service Provider under which they (a) have confidentiality obligations with regard to Synlogic's Confidential Information (as defined in Section 6) that are consistent with the terms of this Agreement; and (b) assign and effectively vest in Service Provider any and all rights that such personnel might have in the results of their work without any obligation of Synlogic to pay any royalties or other consideration to such Service Provider Personnel.

3.5 Compliance. Service Provider will perform all Services with requisite care, skill and diligence, in accordance with all applicable laws, rules, regulations, orders and industry standards. Without limiting Service Provider's obligation to comply with all applicable laws and regulations in providing Services, Service Provider agrees to comply with the United States Foreign Corrupt Practices Act, as amended from time to time, and the OECD Anti-Bribery Convention with regard to Services including not offering or giving anything of value to a foreign public official in connection with the performance of the official's duties or inducing an official to use their position to influence any acts or decisions of any foreign, state or public international organization. If specified in a Statement of Work, Services will be rendered in accordance with applicable Good Laboratory Practices (GLP). If Services under a Statement of Work involve animal research, no animals used by Service Provider in any tests will be used for food purposes and all animals will be disposed of in accordance with applicable laws and regulations. In addition, Service Provider will comply with all Synlogic policies and procedures that have been communicated to Service Provider regarding access to and permitted conduct at Synlogic's or its Affiliate's premises.

3.6 Conflicts with Rights of Third Parties. The conduct and provision of Services will not violate any patent, trade secret or other proprietary or intellectual property right of any third party.

3.7 Absence of Debarment. Service Provider, its Affiliates, Service Provider Personnel and each of their respective officers and directors, as applicable: (a) have not been debarred and are not subject to a pending debarment, and will not use in any capacity in connection with Services any person who has been debarred or is subject to a pending debarment, pursuant to section 306 of the United States Food, Drug and Cosmetic Act, 21 U.S.C. § 335a; (b) are not ineligible to participate in any federal and/or state healthcare programs or federal procurement or non-procurement programs (as that term is defined in 42 U.S.C. § 1320a-7b(f)); (c) are not disqualified by any government or regulatory authorities from performing specific services, and are not subject to a pending disqualification proceeding; and (d) have not been convicted of a criminal offense related to the provision of healthcare items or services and are not subject to any such pending action. Service Provider will notify Synlogic immediately if Service Provider, its Affiliates, any Service Provider Personnel, or any of their respective officers or directors, as applicable, is subject to the foregoing, or if any action, suit, claim, investigation, or proceeding relating to the foregoing is pending, or to the best of Service Provider's knowledge, is threatened.

4. Compensation. As full consideration for Services, Synlogic will pay Service Provider the amounts set forth in the applicable Statement of Work in accordance with the payment schedule set forth in such Statement of Work. Synlogic will have no obligation to pay for any Services (including expenses) that are not set forth in a signed Statement of Work, as amended by any Change Order that is signed or approved (as set forth in Section 2.2). Service Provider will invoice Synlogic for all amounts due in United States Dollars. All undisputed payments will be made by Synlogic within [***] after its receipt of an invoice and reasonable supporting documentation for such invoice.

5. Proprietary Rights.

5.1 Materials. All documentation, information, and biological, chemical or other materials controlled by Synlogic and furnished to Service Provider by or on behalf of Synlogic (collectively, with all associated intellectual property rights, the **"Materials"**) will remain the exclusive property of Synlogic. Service Provider will use Materials only as necessary to perform Services. Service Provider will not analyze Materials except as necessary to perform Services and will not transfer or make the Materials available to third parties without the prior written consent of Synlogic.

5.2 Deliverables.

(a) Ownership. Synlogic will own all rights throughout the world to all inventions, discoveries, improvements, ideas, processes, formulations, products, computer programs, works of authorship, databases, trade secrets, know-how, information, data, documentation, reports, research, creations and all other products and/or materials arising

from or made in the performance of Services (whether or not patentable or subject to copyright or trade secret protection) (collectively, with all associated intellectual property rights, the **"Deliverables"**). Service Provider will assign and does assign to Synlogic all right, title and interest in and to all Deliverables and will promptly disclose to Synlogic all Deliverables. For purposes of the copyright laws of the United States, Deliverables constitute "works made for hire," except to the extent such Deliverables cannot by law be "works made for hire".

(b) Cooperation. During and after the term, Service Provider will, and will cause its Affiliates and Service Provider Personnel to, (i) cooperate fully in obtaining patent and other proprietary protection for any patentable or protectable Deliverables, all in the name of Synlogic and at Synlogic's cost and expense; and (ii) execute and deliver all requested applications, assignments and other documents, and take such other measures as Synlogic reasonably requests, in order to perfect and enforce Synlogic's rights in the Deliverables. Service Provider appoints Synlogic its attorney to execute and deliver any such documents on behalf of Service Provider, its Affiliates, and Service Provider Personnel in the event Service Provider, its Affiliates, or Service Provider Personnel fail to do so.

(c) Service Provider Property. Notwithstanding the foregoing, Service Provider will retain full ownership rights in and to all templates, programs, methodologies, processes, technologies and other materials developed or licensed by Service Provider and its Affiliates prior to or apart from performing its obligations under this Agreement (collectively, with all associated intellectual property rights, the **"Service Provider Property"**), regardless of whether such Service Provider Property is used in connection with Service Provider's performance of its obligations under this Agreement. Service Provider will grant and does grant to Synlogic and its Affiliates a perpetual, non-exclusive, fully paid-up worldwide, sublicensable license to use Service Provider Property as required for Synlogic and its Affiliates to use the Deliverables.

5.3 Work at Third Party Facilities. Service Provider agrees not to accept or use any funds, space, personnel, facilities, equipment or other resources of a third party in performing Services or take any other action that could result in a third party owning or having a right in any Deliverables.

5.4 Records; Records Storage. Service Provider will maintain all materials, data and documentation obtained or generated by Service Provider in the course of preparing for and providing Services, including computerized records and files (collectively, the **"Records"**) in a secure area reasonably protected from fire, theft and destruction. All Records, other than financial records of Service Provider, will be the property of Synlogic. Service Provider will not transfer, deliver or otherwise provide any Records to any party other than Synlogic or its Affiliates, without the prior written approval of Synlogic.

5.5 Record Retention. All Records will be retained by Service Provider for a minimum period of three (3) years following completion of the applicable Statement of Work, or longer if required by applicable law or regulation. Service Provider will, at the direction and written request of Synlogic, promptly deliver Records to Synlogic or its designee, or dispose of the Records, unless the Records are required to be retained by Service Provider by applicable law or regulation or for insurance purposes. In no event will Service Provider dispose of any Records without first giving Synlogic sixty (60) days' prior written notice of its intent to do so.

5.6 Restrictions on Use.

(a) The following definitions apply for the purposes of this Section 5.6:

(i) **"Original Material"** means all [***] or other chemical or biological material supplied by Synlogic to Service Provider to perform the Services.

(ii) **"Modifications"** means any substances created by Service Provider, which alter the Original Material in any way, produce alternative forms of the Original Material, or contain or incorporate any form of the Original Material (including Original Material, Progeny or Unmodified Derivatives).

(iii) **"Progeny"** means unmodified descendant from the Original Material (for example, virus from virus, cell from cell, or mouse from mouse).

(iv) **"Unmodified Derivatives"** means substances created by Service Provider, which constitute an unmodified functional subunit or product expressed by the Original Material (for example, [***]).

(b) Without limiting the generality of Section 5.1 and except to the extent required to perform the Services, Service Provider will not:

(i) make any derivative, Unmodified Derivatives, or Modifications of the Original Material or Progeny, without the express written consent of Synlogic;

(ii) modify, analyze or reverse engineer, or attempt to discover the composition or other characteristics of, the Original Material or Progeny, including without limitation, performing tests or experiments with a view towards generating information based on which a determination of composition or other characteristics could be made, conduct genetic analysis or make genetic manipulation or other alterations on the Original Material or Progeny, chemically or genetically modify the Original Material or Progeny, or otherwise alter or modify its composition;

(iii) perform any experiments with any Original Material.

(iv) use the Original Material, Modifications or Confidential Information for any commercial purposes;

(v) use the Original Material, Progeny or Modifications in human subjects, whether in clinical trials or otherwise and whether for therapeutic, preventive, diagnostic or other purposes;

(vi) use the Original Material, Progeny, Modifications or Confidential Information in research projects that grant or may grant a sublicense, ownership or other proprietary rights in the Original Material, Progeny, Modifications or Confidential Information to a third party; or

(vii) provide or make available to anyone outside of Service Provider's direct supervision, or to any third party for any purpose whatsoever the Original Material, Progeny, Confidential Information or Modifications without the prior written consent of Service Provider whose consent may be withheld at its sole discretion.

6. Confidentiality.

6.1 Definition. **"Confidential Information"** means any and all non-public scientific, technical, financial, regulatory or business information, or data or trade secrets in whatever form (written, oral or visual) that is (a) furnished or made available by or on behalf of one party (the **"Discloser"**) to the other (the **"Recipient"**) or developed by Service Provider in connection with Services; and (b) if Service Provider is the Discloser, such information (i) if in tangible form, is labeled in writing as proprietary or confidential; or (ii) if in oral or visual form, is identified as proprietary or confidential at the time of disclosure or within fifteen (15) days after such disclosure. Confidential Information of Synlogic includes (x) Materials, Deliverables and Records; (y) development and marketing plans, regulatory and business strategies, financial information, and forecasts of Synlogic; and (z) all information of third parties that Synlogic has an obligation to keep confidential, whether or not, in each case, such materials or information are marked or identified as confidential.

6.2 Obligations. During the term of this Agreement and for a period of five (5) years thereafter (and in the case of trade secrets, until such time as Discloser no longer treats such information as a trade secret), Recipient agrees to (a) hold in confidence all Discloser's Confidential Information, and not disclose Discloser's Confidential Information except as expressly provided in Section 6.3, without the prior written consent of Discloser; (b) use Discloser's Confidential Information solely to carry out Recipient's rights or obligations under this Agreement; (c) treat Discloser's Confidential Information with the same degree of care Recipient uses to protect Recipient's own confidential information but in no event with less than a reasonable degree of care; (d) reproduce Discloser's Confidential Information solely to the extent necessary to carry out Recipient's rights or obligations under this Agreement, with all such reproductions being considered Discloser's Confidential Information; and (e) notify Discloser of any unauthorized disclosure of Discloser's Confidential Information, promptly upon becoming aware of such disclosure.

6.3 Permitted Disclosures. Recipient may provide Discloser's Confidential Information to its Affiliates, and to its and their directors, employees, consultants, contractors and agents (but if Recipient is Service Provider, then solely to Service Provider Personnel who are in compliance with Section 3.4) on a need to know basis and solely as necessary to carry out Recipient's rights or obligations under this Agreement; *provided,* that (a) Recipient remains liable for the compliance of such Affiliates, directors, employees, consultants, contractors and agents with the terms of this Agreement and (b) in the case of Service Provider, such disclosure is only to the extent necessary for Service Provider to carry out its obligations under this Agreement. Recipient may also disclose Discloser's Confidential Information to third parties only to the extent such disclosure is required to (i) to comply with (x) applicable law, (y) regulation or (z) the rules of any stock exchange or listing entity; (ii) to defend or prosecute litigation; or (iii) by a governmental authority or by order of a court of competent jurisdiction; *provided,* that Recipient provides prior written notice of such disclosure to Discloser, takes all reasonable and lawful actions to avoid or minimize the degree of such disclosure, and cooperates reasonably with Discloser in any efforts to seek a protective order. Furthermore, Synlogic may disclose Confidential Information of Service Provider relating to Services to entities with whom Synlogic has (or may have) a strategic product marketing and/or development collaboration or to bona fide actual or prospective underwriters, investors, lenders or other financing sources or to potential acquirers of the business to which this Agreement relates, and who in each case have a specific need to know such Confidential Information and who are bound by a like obligation of confidentiality and restrictions on use.

6.4 Exceptions. Recipient's obligations of non-disclosure and non-use under this Agreement will not apply to any portion of Discloser's Confidential Information that Recipient can demonstrate, by competent proof:

(a) is generally known to the public at the time of disclosure or becomes generally known through no wrongful act on the part of Recipient;

(b) is in Recipient's possession at the time of disclosure other than as a result of Recipient's breach of any legal obligation;

(c) becomes known to Recipient on a non-confidential basis through disclosure by sources other than Discloser having the legal right to disclose such Confidential Information; or

(d) is independently developed by Recipient without reference to or reliance upon Discloser's Confidential Information.

6.5 Personal Identifiable Information. Notwithstanding anything to the contrary in this Section 6, (a) Service Provider will not disclose to any third party nor use any protected health information, personal data or biological samples of subjects enrolled in clinical studies that are the subject of Services (collectively, **"Personal Identifiable Information"**) except as expressly required in the applicable Statement of Work and as long as such disclosure and use is in

compliance with applicable law; and (b) such restrictions on the disclosure and use of Personal Identifiable Information will remain in place for as long as such restrictions are required under applicable law. Synlogic's use and disclosure of Personal Identifiable Information will be in accordance with applicable laws and regulations and the relevant consent documents.

7. Indemnification; Insurance; Remedies.

7.1 Indemnification by Service Provider. Service Provider will indemnify, defend and hold harmless Synlogic, its Affiliates, and its and their respective officers, directors, employees and agents (collectively, the **"Synlogic Indemnitees"**) [***], to the extent such claims arise out of or relate to (a) [***] (as defined in Section 7.2) [***]

7.2 Indemnification by Synlogic. Synlogic will indemnify, defend and hold harmless Service Provider, its Affiliates, and its and their respective officers, directors, employees and agents (collectively, the **"Service Provider Indemnitees"**) [***], to the extent such claims arise out of or relate to (a) [***]

7.3 Indemnification Procedures. Each party must notify the other party within [***] after receipt of any claims made for which the other party might be liable under Section 7.1 or 7.2, as applicable. The indemnifying party will have the sole right to defend, negotiate, and settle such claims. The indemnified party will be entitled to participate in the defense of such matter and to employ counsel at its expense to assist in such defense; *provided, however,* that the indemnifying party will have final decision-making authority regarding all aspects of the defense of the claim. The indemnified party will provide the indemnifying party with such information and assistance as the indemnifying party may reasonably request, at the expense of the indemnifying party. Neither party will be responsible nor bound by any settlement of any claim or suit made without its prior written consent; *provided, however,* that the indemnified party will not unreasonably withhold or delay such consent.

7.4 Insurance. During the term of this Agreement and for a period of at least two (2) years after termination or expiration of this Agreement, Service Provider will maintain the following minimum insurance coverage with financially sound and nationally reputable insurers: Workers Compensation (applicable statutory limits); Commercial General Liability including contractual liability ($1,000,000 per occurrence/$2,000,000 aggregate); Comprehensive Automobile Liability ($1,000,000); Professional Liability/Errors and Omissions ($1,000,000 per occurrence); and Umbrella liability coverage ($5,000,000 per occurrence/$5,000,000 aggregate). Service Provider will name Synlogic as an additional insured (except on policies for Workers' Compensation) and will provide Synlogic with a Certificate of Insurance evidencing such coverages naming Synlogic as an additional insured and providing that thirty (30) days' advance written notice will be given to Synlogic of any material change or cancellation in coverage or limits.

7.5 Remedies. In the event that any Services do not meet the specifications or other performance criteria agreed to by Service Provider and Synlogic in writing, then Service Provider will, at Synlogic's option, promptly (a) re-perform such Services at Service Provider's cost; or (b) refund to Synlogic all amounts paid by Synlogic to Service Provider in connection with such Services. Further, Service Provider agrees that (i) Synlogic may be irreparably injured by a breach of this Agreement; (ii) money damages would not be an adequate remedy for any such breach; and (iii) Synlogic will be entitled to seek equitable relief, including injunctive relief and specific performance, without having to post a bond, as a remedy for any such breach. The provisions of this Section 7.5 are not exclusive, and Synlogic may seek any other right or remedy that it may have under this Agreement or otherwise.

8. Expiration; Termination.

8.1 Expiration. This Agreement will expire on the later of (a) three (3) years from the Effective Date or (b) the completion of all Services under all Statement(s) of Work executed by the parties prior to the third anniversary of the Effective Date. This Agreement may be extended by mutual agreement of the parties or earlier terminated in accordance with Section 8.2 or 8.3.

8.2 Termination by Synlogic. In the event of a breach of this Agreement by Service Provider which cannot be cured *(e.g.,* breach of confidentiality obligations under Section 6), Synlogic may terminate this Agreement or any Statement of Work with immediate effect, at any time upon written notice to Service Provider. Further, Synlogic may terminate this Agreement or a Statement of Work at any time upon [***] prior written notice to Service Provider.

8.3 Termination by Service Provider. Service Provider may terminate this Agreement or any Statement of Work if Synlogic fails to cure a material breach of this Agreement or of a Statement of Work within [***] after receiving written notice from Service Provider of such breach.

8.4 Effect of Termination or Expiration. Upon termination or expiration of this Agreement, neither Service Provider nor Synlogic will have any further obligations under this Agreement, or in the case of termination or expiration of a Statement of Work, under that Statement of Work, except that:

(a) Service Provider will terminate all affected Services in progress in an orderly manner as soon as practical and in accordance with a schedule agreed to by Synlogic and, if requested, will work with Synlogic to transition the relevant Services to Synlogic or its designee, unless Synlogic specifies in the notice of termination that Services in progress should be completed;

(b) Service Provider will deliver to Synlogic all Deliverables developed through termination or expiration and will deliver to Synlogic, or at Synlogic's option, dispose of, any Materials in its possession or control;

(c) Synlogic will pay Service Provider any monies due and owing Service Provider, up to the time of termination or expiration, for Services properly performed and all authorized expenses actually incurred (as specified in the applicable Statement of Work);

(d) Service Provider will promptly refund any monies paid in advance by Synlogic for Services not rendered;

(e) each Recipient will promptly return to the Discloser all of Discloser's Confidential Information (including all copies) provided to Recipient under this Agreement or under any Statement of Work which has been terminated or has expired, except for one (1) copy which Recipient may retain solely to monitor Recipient's surviving obligations of confidentiality and non-use, and in the case of Synlogic, to exercise all surviving rights of Synlogic under this Agreement; and

(f) the terms and conditions under Sections 2.3(b), 2.4, 3, 5, 5.6, 6, 7, 8.4 and 9 will survive any such termination or expiration.

9. Miscellaneous.

9.1 Independent Contractor. Service Provider is an independent contractor and not an agent or employee of Synlogic. Service Provider will not in any way represent itself to be an agent, employee, partner or joint venturer of or with Synlogic, and Service Provider has no authority to obligate or bind Synlogic by contract or otherwise. Service Provider has full power and authority to determine the means, manner and method of performance of Services. Service Provider is responsible for, and will withhold and/or pay, any and all applicable federal, state or local taxes, payroll taxes, workers' compensation contributions, unemployment insurance contributions, or other payroll deductions from the compensation of Service Provider's employees and other Service Provider Personnel and no such employees or other Service Provider Personnel will be entitled to any benefits applicable to or available to employees of Synlogic. Service Provider understands and agrees that it is solely responsible for such matters and that it will indemnify Synlogic and hold Synlogic harmless from all claims and demands in connection with such matters.

9.2 Publicity. Except to the extent required by applicable law or regulation or the rules of any stock exchange or listing agency, Service Provider will not make any public statement or release concerning this Agreement or the transactions contemplated by this Agreement or use Synlogic's name or the name of any Affiliate of Synlogic in any form of advertising, promotion or publicity, without obtaining the prior written consent of Synlogic.

9.3 Certain Disclosures and Transparency. Service Provider acknowledges that Synlogic and its Affiliates are required to abide by federal and state disclosure laws and certain transparency policies governing their activities including providing reports to the government and to the public concerning financial or other relationships with healthcare providers. Service

Provider agrees that Synlogic and its Affiliates may, in their sole discretion, disclose information about this Agreement and about Service Provider's Services including those relating to healthcare providers and any compensation paid to healthcare providers pursuant to this Agreement. Service Provider agrees to promptly supply information reasonably requested by Synlogic for disclosure purposes. To the extent that Service Provider is independently obligated to disclose specific information concerning Services relating to healthcare providers and compensation paid to healthcare providers pursuant to this Agreement, Service Provider will make timely and accurate required disclosures.

9.4 Notices. All notices must be in writing and sent to the address for the recipient set forth in this Agreement or at such other address as the recipient may specify in writing under this procedure. Communications and notices to Synlogic will be marked "Attention: Legal Department" with a copy to Naimesh Kotadia, Manufacturing Lead. Communications and notices to Service Provider will be marked "Attention: Ravi Samavedam, General Manager". All notices must be given (a) by personal delivery, with receipt acknowledged; or (b) by prepaid certified or registered mail, return receipt requested; or (c) by prepaid recognized express delivery service. Notices will be effective upon receipt or at a later date stated in the notice.

9.5 Assignment. Except as expressly provided in Section 2.3, Service Provider may not assign, delegate or transfer its obligations under this Agreement, in whole or in part, without the prior written consent of Synlogic, and any attempted assignment, delegation or transfer by Service Provider without such consent will be void. Synlogic may assign, delegate or transfer this Agreement in whole or in part without consent of Service Provider. No assignment, delegation or transfer will relieve either party of the performance of any accrued obligation that such party may then have under this Agreement.

9.6 Entire Agreement. This Agreement, together with the attached Appendix A and any fully-signed Statements of Work, each of which are incorporated into this Agreement, constitute the entire agreement between the parties with respect to the specific subject matter of this Agreement and all prior agreements, oral or written, with respect to such subject matter are superseded. Each party confirms that it is not relying on any representations or warranties of the other party except as specifically set forth in this Agreement. If there is any conflict, discrepancy or inconsistency between the terms of this Agreement and any Statement of Work, purchase order or other form used by the parties, the terms of this Agreement will control.

9.7 No Modification. This Agreement (including Statement(s) of Work) may be changed only by a writing signed by authorized representatives of each party.

9.8 Severability; Reformation. Each provision in this Agreement is independent and severable from the others, and no provision will be rendered unenforceable because any other provision is found by a proper authority to be invalid or unenforceable in whole or in part. If any provision of this Agreement is found by such an authority to be invalid or unenforceable in whole or in part, such provision will be changed and interpreted so as to best accomplish the objectives of such unenforceable or invalid provision and the intent of the parties, within the limits of applicable law.

9.9 Governing Law. This Agreement and any disputes arising out of or relating to this Agreement will be governed by, construed and interpreted in accordance with the internal laws of the Commonwealth of Massachusetts, without regard to any choice of law principle that would require the application of the law of another jurisdiction. The parties expressly reject any application to this Agreement of (a) the United Nations Convention on Contracts for the International Sale of Goods; and (3) the 1974 Convention on the Limitation Period in the International Sale of Goods, as amended by that certain Protocol, done at Vienna on April 11, 1980.

9.10 Jurisdiction; Venue. Any legal action or proceeding concerning the validity, interpretation and enforcement of this Agreement, matters arising out of or related to this Agreement or its making, performance or breach, or related matters will be brought exclusively in the courts of the Commonwealth of Massachusetts. All parties consent to the exclusive jurisdiction of those courts and waive any objection to the propriety or convenience of such venues.

9.11 Waivers. Any delay in enforcing a party's rights under this Agreement, or any waiver as to a particular default or other matter, will not constitute a waiver of such party's rights to the future enforcement of its rights under this Agreement, except with respect to an express written waiver relating to a particular matter for a particular period of time signed by an authorized representative of the waiving party, as applicable.

9.12 No Strict Construction; Headings; Interpretation. This Agreement has been prepared jointly and will not be strictly construed against either party. The section headings are included solely for convenience of reference and will not control or affect the meaning or interpretation of any of the provisions of this Agreement. The words "include," "includes" and "including" when used in this Agreement (and any Statement(s) of Work) are deemed to be followed by the phrase "but not limited to".

9.13 Counterparts. This Agreement may be executed in any number of counterparts, each of which will be deemed to be an original and all of which together will constitute one and the same instrument. A facsimile or portable document format (".pdf") copy of this Agreement, including the signature pages, will be deemed an original.

[Remainder of page left blank intentionally]

IN WITNESS WHEREOF, each party has caused this Agreement to be executed by its duly authorized representative as of the Effective Date.

SYNLOGIC OPERATING COMPANY, INC.		**AZZUR GROUP, D/BA AZZUR OF NEW ENGLAND LLC**	
By:	/s/ Todd Shegog	By:	/s/ Ravi Samavedam
Print Name:	Todd Shegog	Print Name:	RAVI SAMAVEDAM
Title:	CFO	Title:	GENERAL MANAGER

APPENDIX A

SAMPLE STATEMENT OF WORK

THIS STATEMENT OF WORK (the **"Statement of Work"**) by and between **Synlogic Operating Company, Inc. ("Synlogic") and Azzur Group (d/b/a Azzur of New England LLC) ("Service Provider"),** will be effective as of the last date of signature below, and upon execution will be incorporated into the Master Contract Services Agreement between Synlogic and Service Provider dated 08 September 2018 (the **"Agreement"**). Capitalized terms used in this Statement of Work will have the same meaning as set forth in the Agreement.

Synlogic hereby engages Service Provider to provide Services, as follows:

1. **Services.** Service Provider will provide the following Services to Synlogic:

Describe specific Services to be provided including all Deliverables. Also include, as applicable, format of data Deliverables, procedures for verification of accuracy of data, and whether Services must be performed in accordance with GLP, etc.

2. **Materials**. Synlogic will provide to Service Provider the following Materials for Services:

Describe specific materials being provided by Synlogic.

3. **Completion**. Services will be completed [within [TIME PERIOD].] or [in accordance with the following schedule: [INSERT SCHEDULE]]

4. **Service Provider Contacts**.

Project Leader: [NAME AND TITLE]

Administration Contact: [NAME AND TITLE]

Payment Contact: [NAME AND TITLE]

5. **Key Service Provider Personnel**.

Identify all Key Service Provider Personnel, if any (see Section 2.5 (Key Service Provider Personnel) of the Agreement). If none, so state.

6. **Synlogic Representative**. [NAME AND TITLE]

7. **Compensation**. The total compensation due Service Provider for Services under this Statement of Work will not exceed [WRITTEN AMOUNT (numerical amount)]. All amounts due under this Statement of Work will be invoiced in United States Dollars to the attention of [NAME AND TITLE] as follows: [INVOICE SCHEDULE]. All pass through costs must be approved in advance in writing by Synlogic and will not include any

administrative or other additional charges. Amounts due for pass through costs will be invoiced in the billing cycle first following the date they are incurred and invoices will indicate which costs are pass through costs. Payment will be made in accordance with Section 4 (Compensation) of the Agreement. Service Provider agrees that the amounts payable or otherwise provided by Synlogic under this Agreement represent the fair market value of the Services and have not been determined in a manner that takes into account the volume or value of any referrals or business.

All terms and conditions of the Agreement will apply to this Statement of Work. In the event of any conflict between this Statement of Work and the terms of the Agreement, the terms of the Agreement will control. A facsimile or portable document format (".pdf) copy of this Statement of Work, including the signature pages, will be deemed an original.

[Remainder of page left blank intentionally]

STATEMENT OF WORK AGREED TO AND ACCEPTED BY:

SYNLOGIC OPERATING COMPANY, INC.		**AZZUR GROUP, D/BA AZZUR OF NEW ENGLAND LLC**	
By:	_____	By:	_____
Print Name:	_____	Print Name:	_____
Title:	_____	Title:	_____
Date:	_____	Date:	_____

CONFIDENTIAL **Exhibit 10.30**

Proposal P-6454 (SOW No. 1) For

Statement of Work for Suite 1 Rental

THIS STATEMENT OF WORK (the "Statement of Work") by and between Synlogic Operating Company, Inc. ("Synlogic") and Azzur Group (d/b/a Azzur of New England LLC) ("Service Provider"), will be effective as of the last date of signature below, and upon execution will be incorporated into the Master Contract Services Agreement between Synlogic and Service Provider dated 08 September 2018 (the "Agreement"). Capitalized terms used in this Statement of Work will have the same meaning as set forth in the Agreement.

Portions of this Exhibit, indicated by the mark "[***]", were omitted and have been filed separately with the Secretary of the Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

CONFIDENTIAL

Table of Contents

Portions of this Exhibit, indicated by the mark "[***]", were omitted and have been filed separately with the Secretary of the Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

CONFIDENTIAL
Proposal for Facility Use and Professional Services (SOW No. 1)

Section 1 – Background/Scope

Upon execution of this Statement of Work No. 1 and initiation of a purchase order, Azzur will commence performing this Services set forth in this Statement of Work No. 1. The existence and terms of this agreement shall be considered Confidential Information (as that term is used in the Agreement). Azzur will not subcontract use of the cleanroom or the performance of any Services under this Statement of Work No. 1 to a 3rd party without Synlogic's written approval. This Statement of Work No. 1 is for the use of Azzur of New England LLC's Waltham facility, including the cleanroom, warehouse and raw materials laboratory services as well as professional services such as equipment calibration/qualification, quality support and material handling. This Statement of Work No. 1 includes the following Services and associated costs:

a) Cleanroom Use and Associated Costs

b) Warehousing Use and Associated Costs: [***]

c) Warehousing Use and Associated Costs: Use of process gases, [***] and shipping

d) Performance of calibration/qualification of equipment planned for use in early phase clinical manufacturing

e) Personnel Support

The scope of this Statement of Work No. 1 does not include procurement/purchase of equipment, raw materials, consumables etc. on behalf of Synlogic. Any such items will be invoiced to Synlogic at cost plus a processing/handling/storage fee of [***]**.**

Several assumptions have been made to develop Section 3 of this Statement of Work No. 1, which contains the breakdown of hours and costs for each Service described in this Statement of Work No. 1. Changes to the Services can be addressed via an amendment to this Statement of Work No. 1 or via a change order, in each case executed an authorized representative of each party; provided that Azzur will not incur any additional costs that are not set forth in this Statement of Work No. 1 until an amendment or change order specifying such additional costs is executed by each party.

Section 2 – Technical Requirements

AZZUR personnel will be experienced with FDA facility compliance expectations. AZZUR has based this Statement of Work No. 1 upon the following documents.

- Code of Federal Regulations Title 21 Part 210 – Current Good Manufacturing Practice in the Manufacturing, Processing, Packing, or Holding of Drugs; General
- Code of Federal Regulations Title 21 Part 211 – Current Good Manufacturing Practice for Finished Pharmaceutical

- ASTM E-2500 – 07 – Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment
- ISPE Good Practice Guide – Applied Risk Management for Commissioning and Qualification
- ISPE Good Practice Guide – Science and Risk-Based Approach for the Delivery of Facility Systems and Equipment
- ISPE Good Practice Guide – Good Engineering Practices
- PDA Technical Report 56 – Application of Phase Appropriate Quality System and cGMP to the Development of Therapeutic Protein Drug Substance

Section 3 – Detailed Estimate

a) Cleanroom Use Costs

The proposed cleanroom (Suite 1) for use by Synlogic includes [***].

A copy of the layout diagram of Suite 1 is attached as Exhibit A.

The following items are included in the cost of the cleanroom use:

- Access to qualified/maintained core and gowning areas – Qualified to ISO standards
    - All entry/exit door to classified spaces will be interlocked
    - Room differential pressures will be monitored on a routine basis (at least every 24 hours)
- Cleanroom cleaning
    - Weekly – Horizontal and vertical surfaces including wiped using IPA, floors vacuumed and mopped using the latest version of the following approved cleaning solution [***].
    - Monthly – Same as weekly cleaning followed by second cleaning using approved cleaning solution on all surfaces [***].
    - Quarterly (once every 3 months) – Same as monthly cleaning [***]
    - Triple clean – Quarterly cleaning performed 3 times. Performed on an as needed basis between campaigns or at Synlogic's request.

- Security and badge access control. Facility access to Suite 1 is not restricted, on the basis that Azzur safety policies are met. Personnel may not work as a lone worker outside of regular business hours (Monday – Friday, 0700-1800).
- Back-up power (backup generator in place)
- Routine Environmental Monitoring
    - Weekly TAP, Viable Air and Surface Monitoring – Additional environmental monitoring may be completed upon request as time & materials.
- Utilities
    - Power, water (hand washing sink)
- Pest Control
- Waste Disposal (Biological, Hazardous, Non-Hazardous)
- [***] certification/maintenance for existing [***].
- Any other repair or maintenance on all aspects of the classified space (e.g. HVAC maintenance, routine repairs)

The table below includes the all-inclusive cost of all items listed above. Equipment rental of an additional [***] is also available.

Table 1: Cleanroom Use Costs

Item Description	Per Month	Estimated Total Cost*
Cleanroom Use Costs (Fixed Price)	[***]	[***]
Equipment Rental – additional BSC	[***]	[***]
Total Cost		[***]

*Based on discussions with Synlogic the cleanroom will be used for a duration of 6 months starting November 2018.

Synlogic's personnel using the classified areas are to be trained on Azzur SOPs on gowning, personnel movement, material control etc., costs for such training will be covered under quality personnel costs (Time and Materials).

Any gowns, gloves, wipes and similar disposables supplied by Azzur for Synlogic's use will be invoiced at cost [***] for stocking, storage and handling.

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b) Warehousing Use Costs: Ambient and Cold Storage

The Azzur warehouse is approximately [***], including the receiving/loading dock.

The following items are included in the cost of the warehouse use:

- Escorted access to secure, qualified and monitored warehouse – Qualified/monitored for temp/humidity control, security cameras and badge access is in place.
- [***] storage space – 1 pallet total required.
- [***] storage space – Based on discussions with Synlogic, it is estimated that a total of [***]. All CTUs will be monitored for temperature and trends of such monitoring provided to Synlogic upon request.
- Warehouse cleaning and maintenance – The warehouse will be cleaned on a regular basis and maintained by Azzur. Routine revalidations will be performed per Azzur requirements.
- Back-up power (backup generator in place)
- Utilities
    - Power, water
- Pest Control

The table below includes the all-inclusive cost of all items listed above.

Table 2: [***]

Item Description	Unit Cost Per Month	Estimated Total Cost*
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
Warehouse Use Total Estimated Cost		[***]

* Storage will be used by Synlogic for 7 months starting October 2018.

All storage costs will be invoiced from October 2018 to April 2019, irrespective of use.

c) Warehousing Costs: Use of process gases, [***] and shipping

This section provides the standard costs for use of process gases, [***] and shipping to and from the Azzur site in Waltham.

The following items are included in these costs:

- Access to process gases [***]. Azzur will house and maintain gas cylinders for Synlogic use. Process gases will be piped into the cleanroom for use.
- [***] during processing for freezing step.
- Shipping of materials to and from the Azzur site using an Azzur van

The table below includes the costs of all items listed above for the duration of the project.

Table 3: [***]

Item Description	Unit Cost	Estimated Total Cost**
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
Warehouse Use Total Estimated Cost		[***]

** A total duration of 6 months was used for this estimate (November 2018 to April 2019) A total of [***] per month for the duration of 6 months was used for shipping costs. A total of [***] batches was used for this estimate. Invoices will be based on actual usage.

A total of [***] gas cylinders is estimated for the duration of the campaign; only actual use will be billed, on a full cylinder basis.

d) Calibration/Qualification of equipment planned for use in early phase clinical manufacturing

Azzur is capable of providing calibration services using in-house standards and the Azzur Quality Management System. In addition, Azzur has experienced personnel to perform qualification of equipment and related systems in a compliance manner. The following table is an estimate of the costs related to equipment calibration and qualification of equipment that is not owned by Azzur. Equipment that are Azzur-owned and will be used by Synlogic are not included in the list. Any costs related to calibration and qualification of Azzur-owned equipment will not be charged to Synlogic.

Calibration and qualification costs are based on time and materials and will be invoiced based on actual hours spent of such activities. An average hourly rate of [***] has been used for the estimate of calibration and qualification costs.

Table 4: Equipment Calibration/Qualification Costs

[***]	[***]	[***]						
		[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
Total Cost								[***]

e) Testing Description

Azzur is capable of receiving, sampling, testing and releasing raw materials and consumables (referred together as materials) for use in early phase GMP activities, which, for the avoidance of doubt, will be considered Company Materials. Each material/consumable will have a specification in place for establishing release requirements.

Azzur will be able to perform testing as listed in Table 5. All testing will be billed as time & materials as the QC resource provides support (included in Table 6). The estimated materials are listed, and will be billed within the consumables line item. Consumables are billed at list price [***] for handling fee.

Table 5. Testing Supported at Azzur Waltham

Assay	Estimated Materials
[***]	[***]
[***]	[***]

Any tests required to be outsourced to external labs will be invoiced at cost plus [***] for processing, handling etc. All such testing will be reviewed/approved by Azzur quality prior to release of materials. Invoices for testing will be generated based on actual sampling/testing performed on a biweekly basis.

f) Personnel Costs

Based on the scope of work, it is estimated that Azzur personnel will be required for the duration of the project (7 months total). The responsibilities of these resources are listed below:

Responsibilities of the Project Manager include:

- Primary point of contact with Synlogic for coordination of activities in and out of the suite
- Maintaining schedule for calibration/qualification of equipment

Responsibilities of the Material Handler include:

- Receipt, inspection, labeling, handling and shipping of Synlogic materials and equipment
- Generation and maintenance of specifications for Synlogic materials
- Point of contact for kitting of materials for Synlogic use
- Track and maintain inventories related to Synlogic

Responsibilities of the Quality resource include:

- Quality oversight of all Azzur/Synlogic activities related to Synlogic materials, equipment and related entities
- Synlogic point of contact for any and all quality related items, including review/approval of all deviations, change controls, specifications, labels, forms and other documents related to Synlogic operations
- Execution of Quality Control-related items such as material specification generation, raw material testing, and final product testing where applicable.
- Execute aseptic technique training for personnel (may be a different resource than the primary QC/QA resource).

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The below table provides the estimated total costs for personnel based on 7 months of total project duration.

Table 6. Personnel Costs

Role	Hrs/Week	Duration (Weeks)	Hourly Rate	Cost
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]				[***]

g) [***]

Following manufacture of drug product, [***] will be generated by Azzur personnel. The final drug product will be stored on-site at Azzur for [***]. The product will be aliquoted at intervals described within the [***], for a total duration of [***]. Project management of the study is also available. Costs associated with the [***] are listed below in Table 7.

Table 7. [***]

Deliverable/Item	Cost	Notes
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
	[***]	[***]
[***]	[***]	[***]
	[***]	[***]
	[***]	[***]
[***]	[***]	[***]
	[***]	[***]
	[***]	[***]
Total Cost	[***]	

Note: Rates are subject to change each calendar year due to market conditions. Notification will be provided prior to any rate increase.

Section 4 – Overall Project Cost

The following table shows the total costs based on the Services set forth in this Statement of Work No. 1, which are estimated costs where indicated. Azzur will begin performing the Services described in this Statement of Work No. 1 after the Effective Date. Changes to this Statement of Work No. 1 can be made via an amendment to this Statement of Work No. 1 or via a change order at any point during the term of this Statement of Work No. 1, in each case executed by an authorized representative or each party.

Table 8: Overall Project Cost Estimate

Category	Source	Unit Cost	Total Costs	Notes/Assumptions
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
		[***]	[***]	
		[***]	[***]	
[***]	[***]	[***]	[***]	[***]
		[***]	[***]	[***]
		[***]	[***]	
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
GRAND TOTAL			**$548,495**	

All invoices for time and materials-based costs will be based on actual usage or hours spent. Time and expense will be invoiced every month against the approved purchase order and will be based on timesheets, which will be provided to Client upon request.

Cleanroom rent, warehouse space, and CTU rentals will be invoiced on the first of the month.

Consumables will be invoiced every month. An updated consumable list will be provided to Azzur prior to storage and will be updated as appropriate.

An initial invoice following acceptance of this proposal will be generated for a deposit of [***] (Table 8) within [***]. The deposit will be applied to the final invoice against the purchase order.

Section 5 – Timeline

The term of this Statement of Work (the "Term") shall commence on the date indicated on the first page of this Agreement (the "Effective Date"), and shall remain in full force and effect until the final completion of the Services as set out in this Statement of Work. For the time-based elements of this Statement of Work (cleanroom use and warehouse use), the Parties shall, five months after the Effective Date, discuss whether to extend the time-based elements and, if so, shall agree on further terms regarding any such extension.

Section 6 – Exhibits

Exhibit A: Cleanroom Layout

Section 7 – Change History

Date	Reason for Change
13Aug2018	Initial Submission
29Aug2018	Revised Submission
10Sep2018	Revised Submission

SOW 1 Generated by (Azzur):

/s/ Nicole Labrecque

Date – 10Sep2018
Name: Nicole Labrecque
Title: Tech Transfer Manager, Azzur Group
Address: 411 Waverley Oaks Rd., #126
Waltham, MA 02452
Phone: [***]
Cell: [***]
Email: [***]
[***]

SOW 1 Accepted by (Synlogic):

/s/ Todd Shegog

Date – 9/10/2018
Name: Todd Shegog
Title: CFO
Address:
Phone:
Cell:
Email:

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[***]
85130695v.1

Exhibit 10.31

Proposal P-6671 (SOW 2 Revision 1) For

Statement of Work for Azzur of New England Facility Use (Suite 3 – May 1, 2019 to December 31, 2022)

P-6671 SOW 2 Rev l for Facility Use (Suite 3 May 2019 to Dec 2022)

CONFIDENTIAL

THIS STATEMENT OF WORK #2 Rev 1 (the "Statement of Work") by and between Synlogic Operating Company, Inc. ("Synlogic") and Azzur Group (d/b/a Azzur of New England LLC) ("Service Provider"), will be effective as of the last date of signature below, and upon execution will be incorporated into the Master Contract Services Agreement between Synlogic and Service Provider dated 08 September 2018 (the "Agreement"). Capitalized terms used in this Statement of Work will have the same meaning as set forth in the Agreement.

Table of Contents

Section 1 – Background/Scope

Upon execution of this Statement of Work and initiation of a purchase order, Azzur will commence performing this Services set forth in this Statement of Work. This Statement of Work is for the use of Azzur of New England LLC's Waltham cleanroom suite 3 that is planned to be built in the existing space located at 411 Waverley Oaks Rd., #126, Waltham, MA 02452 (see Layout Diagram Attached). The proposed clean room 3 is to be appropriately designed to allow for future expansion to include a [***]. Azzur will not subcontract use of cleanroom 3 or the performance of any Services under this Statement of Work to a 3rd party without Synlogic's written approval.

Section 2 – Technical Requirements

AZZUR personnel will be experienced with FDA facility compliance expectations. AZZUR has based this Statement of Work upon the following documents.

- Code of Federal Regulations Title 21 Part 210 – Current Good Manufacturing Practice in the Manufacturing, Processing, Packing, or Holding of Drugs; General
- Code of Federal Regulations Title 21 Part 211 – Current Good Manufacturing Practice for Finished Pharmaceutical
- ASTM E-2500 – 07 – Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment
- ISPE Good Practice Guide – Applied Risk Management for Commissioning and Qualification
- ISPE Good Practice Guide – Science and Risk-Based Approach for the Delivery of Facility Systems and Equipment
- ISPE Good Practice Guide – Good Engineering Practices
- PDA Technical Report 56 – Application of Phase Appropriate Quality System and cGMP to the Development of Therapeutic Protein Drug Substance

Synlogic's personnel using the classified areas are to be trained on Azzur SOPs on gowning, personnel movement, material control etc.

Section 3 – Detailed Estimate

a) Fixed Priced Costs – Cleanroom Use

The proposed cleanroom (Suite 3) for use by Synlogic includes a total of approximately 700 sq ft with [***]. The location of this proposed new cleanroom suite 3 is an expansion into the existing warehouse space located at 411 Waverley Oaks Rd., #126, Waltham, MA 02452.

The following items are included in the cost of the cleanroom use:

- Access to qualified/maintained core and gowning areas – Qualified to ISO standards
    - All entry/exit door to classified spaces will be interlocked
    - Room differential pressures which will meet [***] classification
    - Temperature specification range of [***] with operation specification control of [***]
    - Humidity specification range of [***] with operational control at [***]
    - Differential pressure, temperature and humidity will be continually monitored using a validated controlled environmental monitoring system (CEMS) on a routine basis
- Cleanroom cleaning
    - Weekly – Horizontal and vertical surfaces including wiped using IPA, floors vacuumed and mopped using the latest version of the following approved cleaning solution [***]
    - Monthly – Same as weekly cleaning followed by second cleaning using approved cleaning solution on all surfaces [***]
    - Quarterly (once every 3 months) – Same as monthly cleaning [***]
    - Triple clean – Quarterly cleaning performed 3 times. Performed on an as needed basis between campaigns or at Synlogic's request.
- Security and badge access control
- Back-up power
- Routine Environmental Monitoring

- Weekly TAP, Viable Air and Surface Monitoring – Additional environmental monitoring may be completed upon request as time & materials.

- Utilities
  - Power, water (hand washing sink)
- Pest Control
- Waste Disposal (Biological, Hazardous, Non-Hazardous)
- BSC certification/maintenance
- Any other repair or maintenance on all aspects of the classified space (e.g. HVAC maintenance, routine repairs). Such events will require downtime in terms of operations and will be scheduled based on Synlogic's needs.

b) Fixed Priced Costs – Storage

Storage space is available on a monthly basis and includes the following:

- Dedicated storage location ([***])
- Temperature and humidity will be continually monitored using a validated controlled environmental monitoring system (CEMS) on a routine basis
- Any other repair or maintenance on the [***] storage units will require downtime in terms of operations and will be scheduled based on Synlogic's needs.

The table below includes the all-inclusive fixed costs for cleanroom use and storage costs for each year. [***] Storage costs are based on the requirements provided by Synlogic. All costs listed in the table below are fixed costs that will be invoiced to Synlogic, at the beginning of each month irrespective of actual usage during the given month. Overages in storage space use compared to below amounts per month will be invoiced at the end of each month. The overage costs are the same as the unit costs quoted below. This SOW has been drafted for a total use duration of 44 months starting May 1st, 2019 to December 31st, 2022. The costs quoted include a price increase of [***] year over year to cover for increase in personnel, utilities and other costs.

Table 1: Fixed Costs (Cleanroom Use and Storage)

Type	Unit Cost/mo (2019)	2019 Cost	2020 Cost	2021 Cost	2022 Cost	Totals
[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]

[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]
Totals		[***]	[***]	[***]	[***]	[***]

c) Variable Costs – Personnel Support

Azzur personnel at various levels will support activities including project management, sampling, material receipt/release, inventory control, training and general consulting for the duration of Synlogic's use of cleanroom 3 and associate storage and other use. These costs are variable and will be invoiced every two weeks based on actual time spent on various Synlogic related activities during that period. Timesheets will be provided with all invoices related to personnel costs. Off-hours support will be provided, as needed with advance notice and the costs are the same as detailed below. The costs quoted include a price increase of [***] year over year due to increase in salaries, benefits costs, raises etc. The table below summarized the estimated variable costs for the duration of 44 months.

Table 2: Variable Costs (Personnel Support)

Type	Unit Cost/hr (2019)	Estimated Hrs/mo	2019 Cost	2020 Cost	2021 Cost	2022 Cost	Totals
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
Totals			[***]	[***]	[***]	[***]	[***]

d) Variable Costs – Process Gases, Shipping, Consumables, Liquid Nitrogen

This section provides the standard costs for use of process gases, shipping, consumables and liquid nitrogen at the Azzur site in Waltham.

The following items are included in these costs:

- Access to process gases ([***]). Azzur will house and maintain gas cylinders for Synlogic use. Process gases will be piped into the cleanroom for use.
- [***] during processing for freezing steps.
- Shipping of materials to and from the Azzur site using an Azzur van.

The table below includes the costs of all items listed above for the duration of the project. These costs are variable and will be invoiced at the end of every month based on actual usage during that period. The costs quoted include a price increase of [***] year over year due to increase in

rent, personnel costs, utilities etc. The table below summarized the estimated variable costs for the duration of 44 months.

Table 3: Variable Costs [***]

Type	Unit Cost/Mo (2019)	Estimated Units or events/mo	2019 Cost	2020 Cost	2021 Cost	2022 Cost	Totals
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
Totals			[***]	[***]	[***]	[***]	[***]

*Consumables will be invoiced based on [***] for storage, handling and related costs. Estimated unit cost is an average amount per month.

The below table shows the total estimated project costs based on the fixed and estimated variable costs shown in tables above.

Table 4: Overall Project Cost Estimate for 44 Months

Category	Source	Type and Invoicing	Total Costs	Notes/Assumptions
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
GRAND TOTAL			**$4,785,040**	

Right of First Refusal

Synlogic has the first right of refusal to rent Cleanroom Suite 3 following December 31st, 2022. Each time that Azzur intends to rent Cleanroom Suite 3 to an alternate client party during the 6-month period after December 31, 2022, Azzur will first promptly notify Synlogic and offer the opportunity to rent Cleanroom Suite 3 on substantially similar terms as Azzur offered to the third party. Synlogic will notify Azzur of its decision to rent Cleanroom Suite 3 on substantially similar terms as Azzur offered to the third party within 15 days after receiving Azzur's notice. If Synlogic does not give written notice to Azzur of its intent to rent Cleanroom Suite 3 within such 15-day period, Azzur will be free to rent Cleanroom Suite 3 to such alternate client without further obligation to Synlogic.

Option to Extend

Synlogic has the option to extend beyond the current end date of this SOW (Dec 2022) provided a letter of intent to extend for a minimum of 3 months at least 6 month before the end date and a new SOW for the extension signed at least 3 months prior to the end date.

Early Termination of Contract

At any time during the duration of Cleanroom Suite 3 rental (May 1st, 2019 to December 31st, 2022), if Synlogic anticipates having to terminate this contract for the rental duration early, it will provide a written notice to Azzur at least 4 months in advance of the effective date of the termination.

Option to Sub-lease Cleanroom

At any time during the duration of Cleanroom 3 rental, if Synlogic anticipates not using the Cleanroom 3, a written notice will be provided at least 3 months in advance to the non-occupancy start date, to Azzur. In such an instance, Azzur will make efforts to find an alternate client to occupy the space for the duration that Cleanroom 3 remains unoccupied. Provided an alternate client is available and willing to occupy the space, Azzur will not charge Synlogic for the duration the alternate client is occupying Cleanroom 3. If Azzur is unable to find an alternate client to occupy Cleanroom 3, Azzur will continue to invoice Synlogic based on the terms of this SOW.

Option to use Alternate Cleanroom, Termination in Event Cleanroom Suite 3 is not Available

Azzur shall inform Synlogic within 2 business days of the delivery of the prefabricated cleanroom suite 3 and related equipment for humidity control to Azzur's facility located at 411 Waverley Oaks Rd., #126, Waltham, MA 02452. In the event that the new cleanroom suite 3 is anticipated to not be ready prior to the start date of use (May 1st, 2019), the existing Cleanroom Suite 1 will be offered to Synlogic, at its election, as a back-up option starting July 1st, 2019, on the terms set out in Proposal P-6454 (SOW No. 1). This determination will be made on the later of March 31st, 2019 or 5 business days after notification by Azzur to Synlogic of the delivery of the prefabricated suite 3 and related equipment for humidity control, as set out above. In the event that cleanroom suite 3 is not available to Synlogic on May 1st, 2019, Synlogic shall have the option to terminate this SOW upon notice to Azzur and any deposit paid by Synlogic shall be returned to Synlogic in full within 30 days of such termination. If Synlogic does not exercise its option to terminate the SOW in the event of a delay, the parties agree that any costs relating to cleanroom suite 3 (other than the deposit) shall not be incurred until such time as the cleanroom suite 3 becomes available to Synlogic. The rates of Cleanroom Suite 1 rental will be subject to the terms and conditions outlined in SOW P-6464.

Invoicing

All invoices related to the fixed costs identified in table 1 will be generated at the start of any given month. Any overages in items listed in table 1 will be invoiced at the end of any given month. All invoices related to the variable costs identified in table 2 will be generated once every two weeks based on actual time spent during that period (with timesheets). All invoices related to the variable costs identified in table 3 will be generated every month based on actual usage for any given month. An initial invoice following acceptance of this proposal will be generated for a

deposit of [***] of the first twelve months of fixed costs [***] within [***] of acceptance by Synlogic of this SOW. The deposit will be applied to the three invoices relating to fixed costs for February, March and April 2020. In order for Azzur to invoice the deposit amount, an initial PO for the first twelve months of fixed and variable costs listed in this SOW will be required. This initial PO will for the twelve months spanning May 2019 through April 20120 and amounts to [***]. Additional POs will need to be generated for the subsequent durations listed in this SOW on a twelve months basis, except for the last PO will be for a duration of 8 months in 2022. The below table shows the PO schedule for the entire duration of 44 months from May 2019 to Dec 2022

Table 5: PO Amounts and Schedules

PO Duration	Amount	Need by Date
May 2019 to April 2020	[***]	Upon signing of the SOW
May 2020 to April 2021	[***]	March 31st 2020
May 2021 to April 2022	[***]	March 31st 2021
May 2022 to Dec 2022	[***]	March 31st 2022
Total Amount	**$4,785,040**	

Section 4 – Change History

Date	Reason for Change
22Oct2018	Initial Submission
30Nov2018	Revision 1

SOW Generated by (Azzur):

/s/ Ravi Samavedam

Date – 30Nov2018
Name: Ravi Samavedam
Title: General Manager, Azzur Group
Address: 411 Waverley Oaks Rd. #126
Waltham, MA 02452
Phone: [***]
Cell: [***]
Email: [***]

SOW Accepted by (Synlogic):

/s/ Todd Shegog

Date – 12/7/2018
Name: Todd Shegog
Title: CFO
Address: 301 Binney Street Suite 402 Cambridge, MA 02142
Phone:
Cell: [***]
Email: [***]

[***]

Cleanroom Suite 3 Proposed Expansion is into existing warehouse space of the Azzur site in Waltham.

Exhibit 21.1

SUBSIDIARIES OF SYNLOGIC, INC.

Subsidiary	**Jurisdiction**
Synlogic IBDCo, Inc.	Delaware
Synlogic Operating Company, Inc.	Delaware
Synlogic Securities Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Synlogic, Inc.

We consent to the incorporation by reference in the registration statements (Nos. 333-220841, 333-223798, 333-210466 and 333-207299) on Form S-8 and (Nos. 333-226730 and 333-220948) on Form S-3 of Synlogic, Inc., of our report dated March 12, 2019, with respect to the consolidated balance sheets of Synlogic, Inc. as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, contingently redeemable preferred equity and stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements), which report appears in the December 31, 2018 annual report on Form 10-K of Synlogic, Inc.

/s/ KPMG LLP
Cambridge, Massachusetts
March 12, 2019

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Aoife Brennan, certify that:

1. I have reviewed this annual report on Form 10-K of Synlogic, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2019

By: /s/ AOIFE BRENNAN

Aoife Brennan

President, Chief Executive Officer and Chief Medical Officer

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Todd Shegog, certify that:

1. I have reviewed this annual report on Form 10-K of Synlogic, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2019

By: /s/ Todd Shegog

Todd Shegog

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Synlogic, Inc. (the "Company") on Form 10-K for the period ending December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Aoife Brennan, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 12, 2019

By: /s/ Aoife Brennan

Aoife Brennan

President, Chief Executive Officer and Chief Medical Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Synlogic, Inc. (the "Company") on Form 10-K for the period ending December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Todd Shegog, Chief Financial Officer, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 12, 2019

By: /s/ Todd Shegog

Todd Shegog
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.