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, 2023

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)**

(617) 401-9975

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of exchange on which registered
Common Stock, par value $0.001 per share	SYBX	The 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 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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, 2023, the last business day of the registrant's most recently completed second quarter, was $23.6 million, computed based on the closing price of $6.45 per share on June 30, 2023.

As of March 12, 2024 there were 11,646,977 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 2023 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, 2023.

Auditor Firm Id: 185 Auditor Name: KPMG LLP Auditor Location: Boston, Massachusetts, U.S.

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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:

- our evaluation of strategic alternatives with a goal to enhance stockholder value, including the possibility of a merger or a sale of the Company;
- 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 success of our collaborations with third parties;
- the progress, timing and costs involved in developing manufacturing processes and in manufacturing products, as well as 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, if approved;
- the revenue generated by sales of our product candidates, if approved;
- 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;
- the extent to which our business is adversely impacted by the effects of the coronavirus outbreak (COVID-19) or by other health epidemics or pandemics; 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 biopharmaceutical company advancing novel therapeutics to transform the care of serious diseases. We focus on rare metabolic disorders, with our lead program, labafenogene marselecobac (SYNB1934), studied in Synpheny-3, a global, pivotal Phase 3 study for patients with phenylketonuria (PKU), and SYNB1353, a potential treatment for homocystinuria (HCU). Both PKU and HCU are caused by inborn errors of metabolism, and present significant need for innovation due to limitations of both efficacy and safety in the currently available medical treatment options.

In February 2024, we made the decision to discontinue Synpheny-3, our pivotal study of our lead product candidate, labafenogene marselecobac (SYNB1934), as a potential treatment for PKU. The decision to end Synpheny-3 is based on results of an internal review in advance of an upcoming independent Data Monitoring Committee (DMC) assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. We will now work with the Synpheny-3 clinical trial sites involved to implement the discontinuation. As a result, our current corporate strategy is focused on pursuing strategic initiatives to enhance stockholder value, including but not limited to, a merger or the sale of the Company. Our strategic process is both active and ongoing and includes a range of interactions with transaction counterparties. Thus, we believe it is in our stockholders' best interest to allow sufficient opportunity to pursue and consummate one or more such transactions and to consider additional alternatives that may materialize in the future. However, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

Our early-stage pipeline includes product candidates for enteric hyperoxaluria, gout, and cystinuria, and has been fueled by a reproducible, proprietary approach that creates GI-restricted, oral medicines with new enzymatic pathways designed to consume or produce specific biological targets. We design, develop and manufacture these drug candidates, which are produced by applying genetic engineering to well-characterized probiotics.

Our drug candidates are designed through precise engineering to target validated biological pathways in the pathophysiology of a given disease. By using a probiotic to deliver these new enzymatic pathways, the activity is restricted to the gastrointestinal (GI) tract, avoiding systemic exposure and associated risks that limit the success of other modalities. Our pipeline programs are all based on the same probiotic Escherichia coli Nissle 1917, which provides synergies across programs, as well as more than one hundred years of human dosing experience. Our drug candidates are engineered to be non-colonizing, and fully reversible via GI clearance. These potential biopharmaceuticals are all orally administered, conducive to straightforward shipping, distribution and storage. For manufacturing, our platform leverages processes with familiar foundations, including fermentation and lyophilization, facilitating process design and scale-up, combined with unique and proprietary innovations tailored to our unique products.

Since our founding, based upon technology from the Massachusetts Institute of Technology (MIT) in 2014, we have progressed a pipeline of multiple drug candidates across different stages, including:

- Labafenogene marselecobac (SYNB1934), which was being studied in Synpheny-3, a pivotal, Phase 3 study for the treatment of patients with PKU;
- SYNB1353, a potential treatment for HCU, has achieved proof of mechanism in a Phase 1 study in healthy volunteers;
- Preclinical research activities on a potential drug candidate for cystinuria, a rare, genetic cause of recurrent kidney stones which is also caused by an underlying metabolic disorder;
- SYNB2081, a drug candidate for gout which is in IND-enabling studies; and
- Preclinical research focused on novel, locally-acting, GI-restricted biotherapeutics for indications in inflammatory bowel disease (IBD).

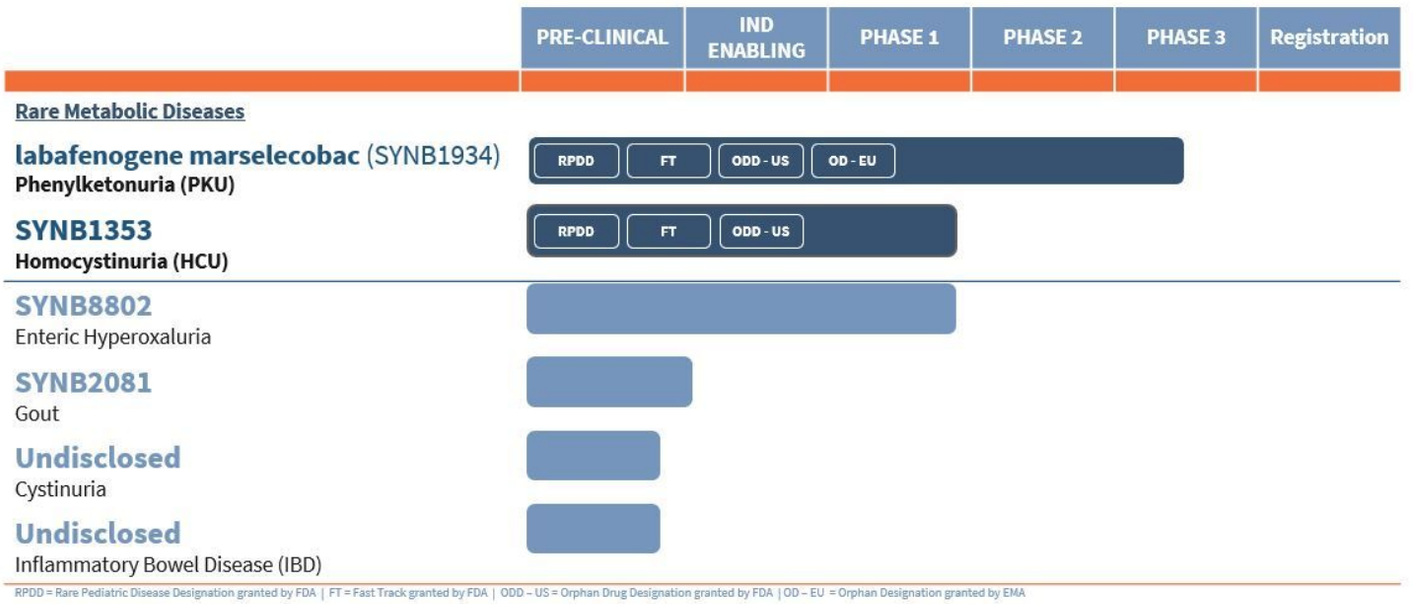
Strategy

As announced in February 2024, our current corporate strategy is focused on pursuing strategic initiatives to enhance stockholder value, including by exploring a range of alternatives including but not limited to a merger or the sale of the Company. Our strategic process is both active and ongoing and includes a range of interactions with transaction counterparties. Thus, we believe it is in our stockholders' best interest to allow sufficient opportunity to pursue and consummate one or more such transactions and to consider additional alternatives that may materialize in the future. However, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

In February 2024, we made the decision to discontinue Synpheny-3, our pivotal study of our lead product candidate, labafenogene marselecobac (SYNB1934), as a potential treatment for PKU. Historically, our mission was to treat diseases underserved by other modalities by researching, developing and commercializing new medicines.

Our Pipeline: Synthetic Biotics in Clinical Development

Our product pipeline consists of drug candidates targeting significant medical needs caused by an underlying metabolic disorder. These include labafenogene marselecobac, which was being evaluated in a pivotal, Phase 3 study in PKU, and drug candidates designed to treat HCU, enteric hyperoxaluria, and gout. Our preclinical work includes additional metabolic disease research, including cystinuria, target exploration, and focused research efforts in IBD.



Clinical Pipeline: Focus on Rare Metabolic Diseases

Rare metabolic diseases often result from inherited defects or alterations in specific enzymes or other biological pathways that normally break down or produce important metabolites or molecules. In patients with these diseases, the absence or impairment of certain enzymes causes potentially toxic metabolites to accumulate. In patients with PKU and HCU, the build-up of these metabolites can reach toxic levels, resulting in life-threatening medical risks and/or serious developmental delays, life-altering disease burden and symptoms. While there are approved and available pharmaceutical products for both diseases, they present significant limitations in terms of both safety and efficacy, leaving patients often under-managed, attempting to control their disease through a restrictive regimen of diet, medical formula and medical foods, and/or experiencing significant symptoms or risk of dangerous complications.

Market Opportunity

In addition to significant need for new medical treatments, we believe rare metabolic diseases PKU and HCU present advantages as target therapeutic areas for investment. Despite their limitations, the approved treatments for these diseases provide useful precedent in terms of both clinical development paths and navigating regulatory processes including approval. For example, in both PKU and HCU, existing treatments were approved by global regulators based on clinical biomarkers as the primary endpoint in their pivotal, registrational trials, sufficient for full approval. All of the metabolic diseases that we target in our current pipeline also

have the benefit of a dietary model, in which there is already a standard dietary intervention to reduce the target metabolite (e.g. avoiding protein in the case of PKU to lower Phe levels, or methionine in the case of HCU, or uric acid for gout). These existing dietary interventions provide a useful model by demonstrating that GI-based means of lowering metabolite levels to provide therapeutic benefit.

From a commercial perspective, these rare metabolic diseases have been well-characterized, and while limited in uptake due to their limitations, the currently available products have provided commercial validation. In PKU for example, the two approved products, Kuvan and Palynziq, have generated $500 million and $300 million respectively, in annual revenue as branded agents, translating to a market opportunity we estimate to be more than $3 billion. For HCU, with an estimated 5,000 patients globally, we estimate a potential market opportunity to be more than $1 billion.

Further, these two disease states present significant synergies as target indications. PKU and HCU patients are largely both treated by the same, concentrated and group of specialist clinicians at metabolic clinics, facilitating both late-stage development and commercialization, given the overlap in key opinion leaders (KOLs), medical meetings and congresses, as well as call points for sales and marketing, market access and patient support programming.

Our PKU Program

Our lead product candidate, labafenogene marselecobac (SYNB1934), which was being evaluated in Synpheny-3, a privotal Phase 3 study, is designed to consume phenylalanine (Phe) through engineered enzymes produced within the probiotic, *E. coli* Nissle. Labafenogene marselecobac has received Orphan Drug Designation (ODD), Fast Track designation, and Rare Pediatric Disease Designation (RPDD) from the FDA in addition to orphan designation from the European Medicines Agency (EMA). In 2023 we announced that the International Nonproprietary Names (INN) Expert Committee of the World Health Organization (WHO-INN) has selected "labafenogene marselecobac" for the nonproprietary name of SYNB1934, reflecting a naming framework for genetically engineered bacteria, in which the first name references the gene being designed or modified (in this case, one for Phe or “fe”), and the second references the bacteria (“bac”).

The Science of PKU

PKU is an inherited metabolic disease caused by genetic mutations that impair the function of the enzyme, phenylalanine hydroxylase (PAH), which normally metabolizes phenylalanine (Phe), an amino acid found in all protein-containing foods, including all meat and dairy products, most beans, grains and potatoes, as well as some artificial sweeteners. Without functioning PAH, uncontrolled Phe levels in PKU can be neurotoxic, interfering with normal brain development during childhood, causing permanent developmental disabilities; severely elevated Phe levels at any age can result in neurocognitive symptoms such as slower cognition, difficulty concentrating or “brain fog.”

Reducing the risk of complications and neurocognitive symptoms in PKU patients requires lifelong control of Phe levels. During the 1960’s, countries began newborn screening to ensure that Phe control was implemented immediately through a highly restrictive, low-Phe diet accompanied by supplemental formula for needed amino acids to avoid permanent, severe intellectual disability. Per E.U. and U.S. guidelines, any newborn infant with a plasma Phe concentration of >400–600 μM should be started on a low-Phe diet as soon as possible. The diet includes extreme restrictions of natural foods to keep daily protein at levels that are often as low as 4-6 grams per day for adults. This generally includes elimination of all sources of animal protein and dairy, legumes and nuts, and limited intake of bread, pasta, rice and some vegetables. Low-protein bread and pasta products made from starch are used to provide needed energy. The dietary regimen required also includes the addition of amino acid-based, Phe-free formula or other specific medical foods to provide adequate protein, vitamins, minerals and energy.

It is challenging for persons to adhere to this restricted diet and its associated requirements create significant burdens on quality of life for both patients and caregivers. Access to low protein foods can pose difficulties as they are costlier and less nutritious than their higher protein, non-modified equivalents, and the needed formula can also be costly or otherwise difficult to access. As a result, the vast majority of people living with PKU, and especially adults living independently, have Phe levels well above the recognized targets.

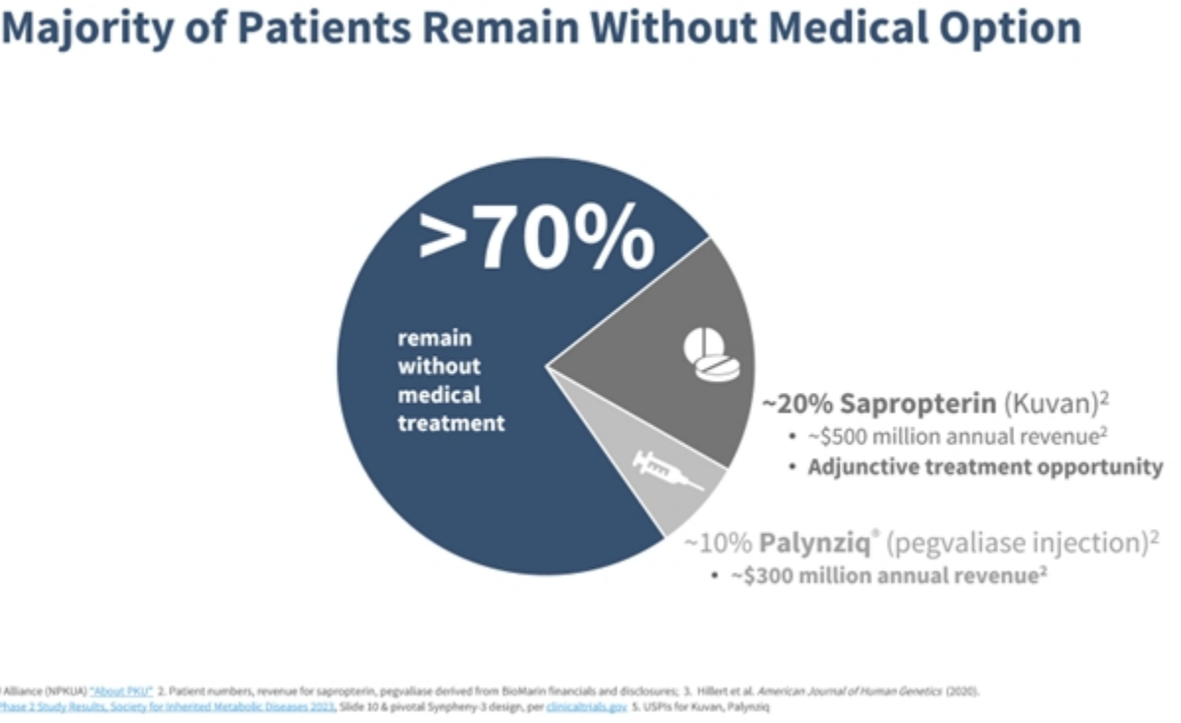
It is estimated that there are more than 150,000 people diagnosed with PKU living across the United States, Europe and Asia. They are typically diagnosed through newborn screening. Of these, the vast majority remain untreated, reflecting the limitations of current treatment options.

Limitiations of Current PKU Treatment Options

There are currently two medications been approved by the FDA, EMA, and other regulatory agencies globally as medical treatments for PKU based on safety and efficacy in reduction of plasma Phe levels. These approved medications provide important and helpful examples and precedents for clinical development and regulatory processes. Each one however, has drawbacks limitations leave the majority of people with PKU living without a medical treatment for Phe reduction. These limitations are outlined below:

- Sapropterin dihydrochloride (Kuvan®), a biopterin, was approved by the FDA in 2017, and is now available as a generic in the United States and other markets in tablet and sachet formulations. Sapropterin works by stimulating the PAH enzyme to process Phe in people with PKU. This requires having residual PAH enzyme, and responding to tetrahydrobiopterin (BH4). Typically only a minority of PKU patients will demonstrate BH4-responsiveness, and as a result, the use of Kuvan has been limited to an estimated 15%-20% of U.S. patients. Reflecting the size of the overall patient population, despite this low use, Kuvan generated ~$500 million per year globally for BioMarin Pharmaceutical, Inc. prior to genericization. Of those who do respond and maintain treatment with sapropterin, we believe a significant proportion would still benefit from additional Phe-lowering, and see this segment as an important opportunity for labafenogene marselecobac as an adjunctive medical treatment option.
- Palynziq® Injection (pegvaliase-pqpz) was approved by the FDA in 2018 for adult patients with PKU and uncontrolled blood Phe. Due to instability and other complexities, the PAH enzyme that is impaired in PKU is not a viable candidate for enzyme replacement therapy. Palynziq is a pegylated form of recombinant phenylalanine ammonia lyase (PAL), a non-mammalian enzyme that also metabolizes Phe. Safety considerations include risk of severe allergic reactions, including a 10% risk of anaphylaxis, resulting in FDA labeling that includes a boxed warning and requirement to carry auto-injectable epinephrine at all times while they are taking the medication. Despite these challenges, Palynziq is forecast to generate $300 million in 2023, largely from the United States, despite maintaining an estimated ~10% market share.

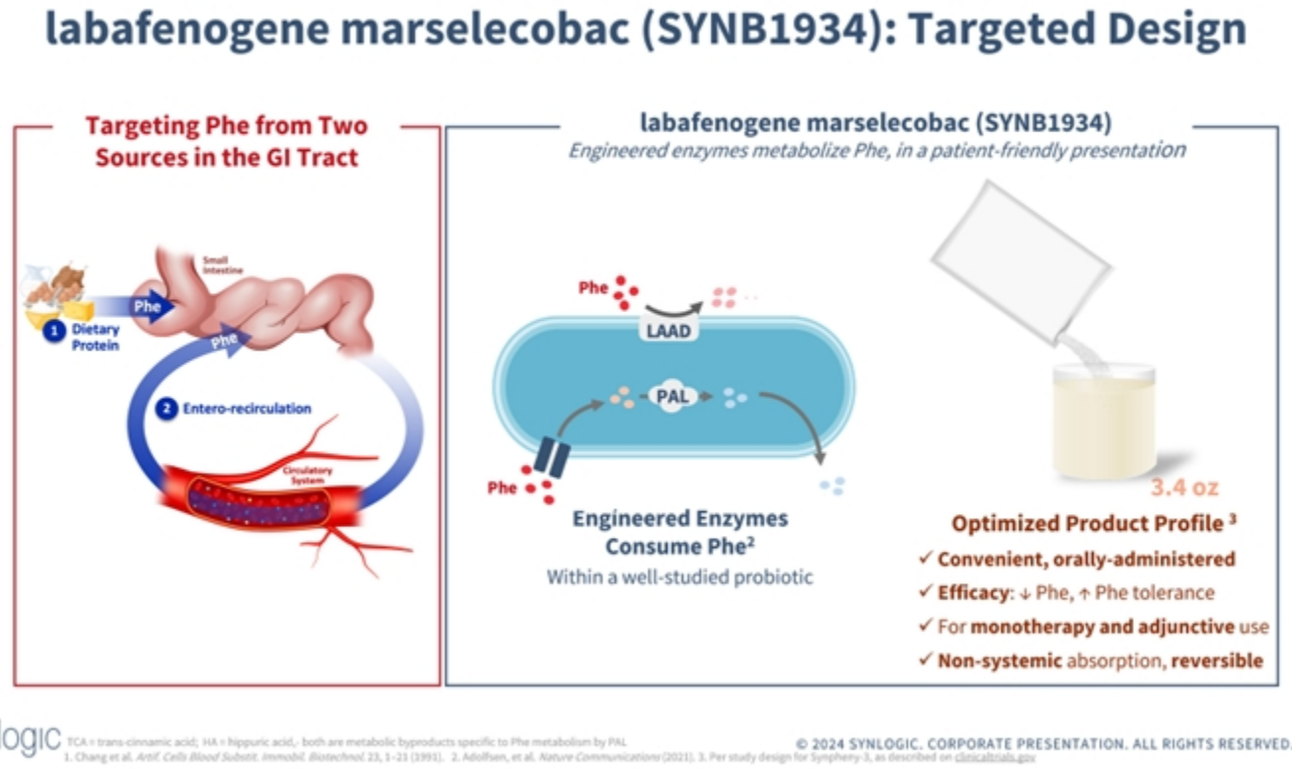
Given the limitations of sapropterin in terms of responder rates, and the safety challenges of Palynziq, we believe the approved therapies' limitations leave a large majority of those living with PKU in need of an orally-administered medical treatment option that provides Phe-lowering efficacy with an acceptable safety and tolerability profile.



Labafenogene marselecobac for PKU

Labafenogene marselecobac is designed to treat PKU and lower Phe levels through the engineering of two Phe-consuming enzymes: L-amino acid deaminase (LAAD) and phenylalanine ammonia lyase (PAL), produced by a strain of *E. coli* Nissle, which also includes a Phe transporter, PheP, to bring Phe into the cell. The drug candidate thustargets Phe from dietary sources, and Phe that has circulated to the GI tract via enterorecirculation.

This design enables a patient-friendly product presentation: it is provided to patients as powder for mixing with water or juice, taken with with meals. This product presentation is familiar to PKU patients, as sapropterin is provided as a sachet, and often their nutritional supplemental formula requires mixing with liquid.

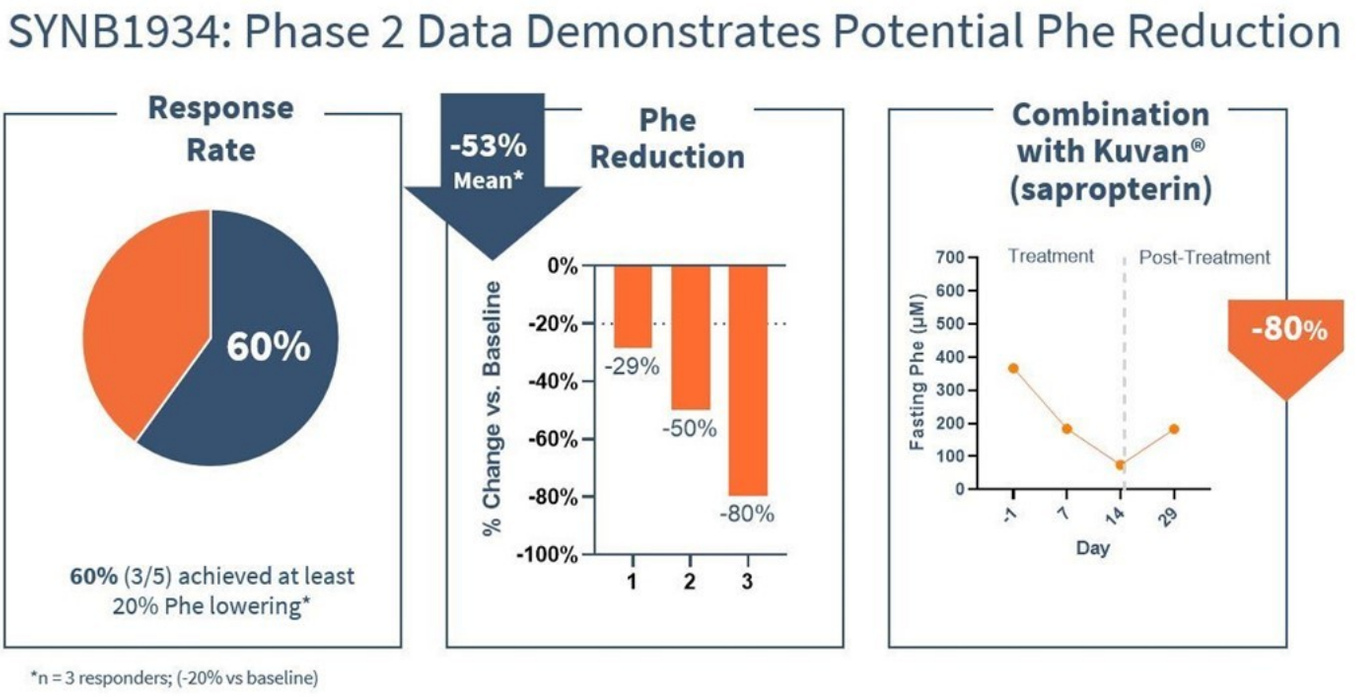


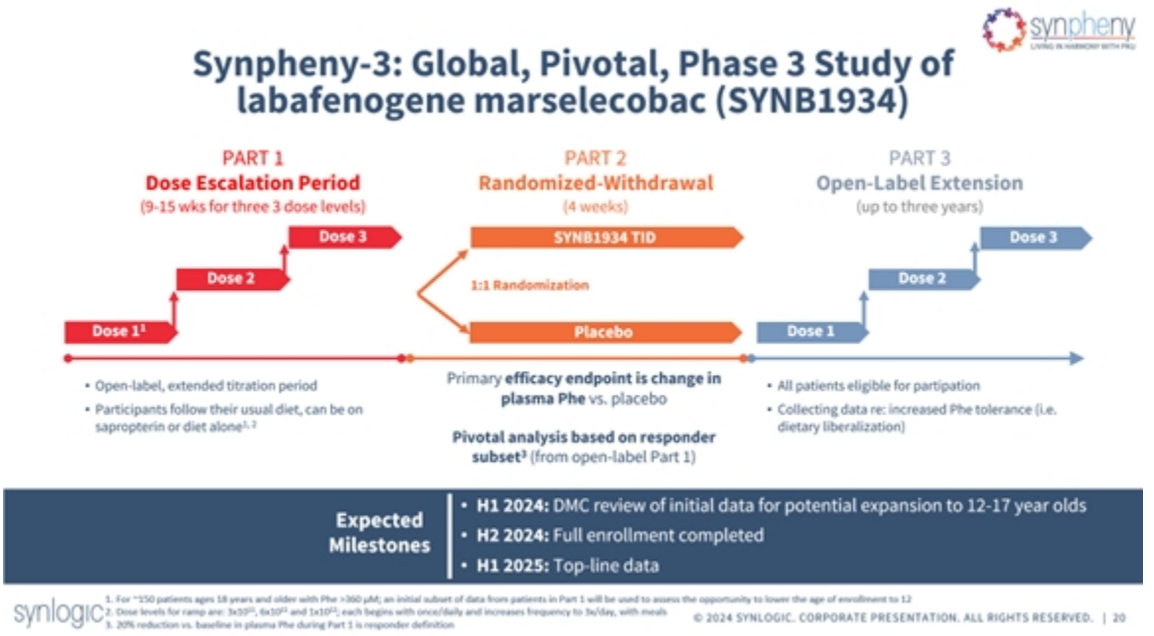
Labafenogene marselecobac was engineered as a next-generation version of first-generation PKU drug candidate SYNB1618, by modifying five amino acids in PAL, which increased productivity of PAL's conversion of Phe to the metabolic byproduct trans-Cinnamic acid (TCA). A detailed description of the engineering of SYNB1618 and data from preclinical studies in an animal model of disease and healthy non-human primates was published in 2018 (Nat. Biotechnol. 36, 857–864 (2018)), and an overview of the engineering and early development of SYNB1934 was published in 2021 (Nat Commun. 12, 6215 (2021)).

In Phase 1 studies of healthy volunteers, both SYNB1618 and labafenogene marselecobac were found to be safe and well-tolerated at doses up to 2x1012 live cells administered three times a day for seven days. Higher doses were associated with mild to moderate gastrointestinal symptoms, mainly nausea and vomiting. In July 2019, we announced data that demonstrated that SYNB1618 was safe and well-tolerated and achieved proof-of-mechanism of strain activity in both healthy volunteers and patients with PKU. Improved tolerability of the lyophilized SYNB1618 over the early liquid formulation enabled us to determine a maximally tolerated dose (MTD) to take forward to test in patients. In September 2021, we announced that Phase 1 results in healthy volunteers and predictive modeling indicate labafenogene marselecobac may have greater potency than SYNB1618.

In October 2022, we shared positive top-line results from the Phase 2 Synpheny-1 study that demonstrated proof of concept in PKU patients for both candidates, and confirmed greater potency of the next-generation labafenogene marselecobac , the candidate that we have selected to advance to pivotal Phase 3 studies. The complete results were presented at the Society for Inherited Metabolic Disorders (SIMD) Annual Meeting in March 2023 and published in the journal Nature Metabolism in September 2023. Results presented included successfully meeting the primary endpoint (change in area under the curve of D5-Phe following a meal challenge) for SYNB1618 and labafenogene marselecobac. Results for labafenogene marselecobac included a -40% mean reduction in plasma Phe levels for labafenogene marselecobac, and -53% among those considered responders (with >20% reduction from baseline). 60% of patients achieved the >20% criteria for Phe reduction considered the threshold for a clinically meaningful response. The study also included experience with both candidates when provided in combination for patients who were already taking sapropterin (Kuvan) at baseline, indicating the potential for adjunctive medical treatment. Safety and tolerability findings were consistent with prior

experience and favorable, with no serious adverse events (SAE) across the PKU program, and those adverse events that did occur being predominantly GI in nature.





In June 2023 we announced the initiation of Synpheny-3. Its design was informed by input from global regulatory agencies, clinicians and patients, and the precedent of pivotal studies from already approved drugs.

The study was a randomized, placebo-controlled, global, pivotal Phase 3 clinical trial designed to evaluate the efficacy and safety of SYNB1934 as a treatment for PKU. The primary endpoint was the change in phenylalanine (Phe) levels from baseline for SYNB1934 compared to placebo, in a subset of patients who are considered responders (defined as >20% reduction in Phe).

The trial consisted of three parts: Part 1, an open-label dose escalation period, during which patients titrate through up to three dose levels, with at least three weeks per dose; Part 2, a four-week randomized withdrawal period used for the pivotal analysis; and Part 3, an open-label extension which includes an evaluation of Phe tolerance, or dietary liberalization.

In February 2024, we made the decision to discontinue Synpheny-3, our pivotal study of our lead product candidate, labafenogene marselecobac (SYNB1934), as a potential treatment for PKU. The decision to end Synpheny-3 is based on results of an internal review in advance of an upcoming independent Data Monitoring Committee (DMC) assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability.

Our HCU Program

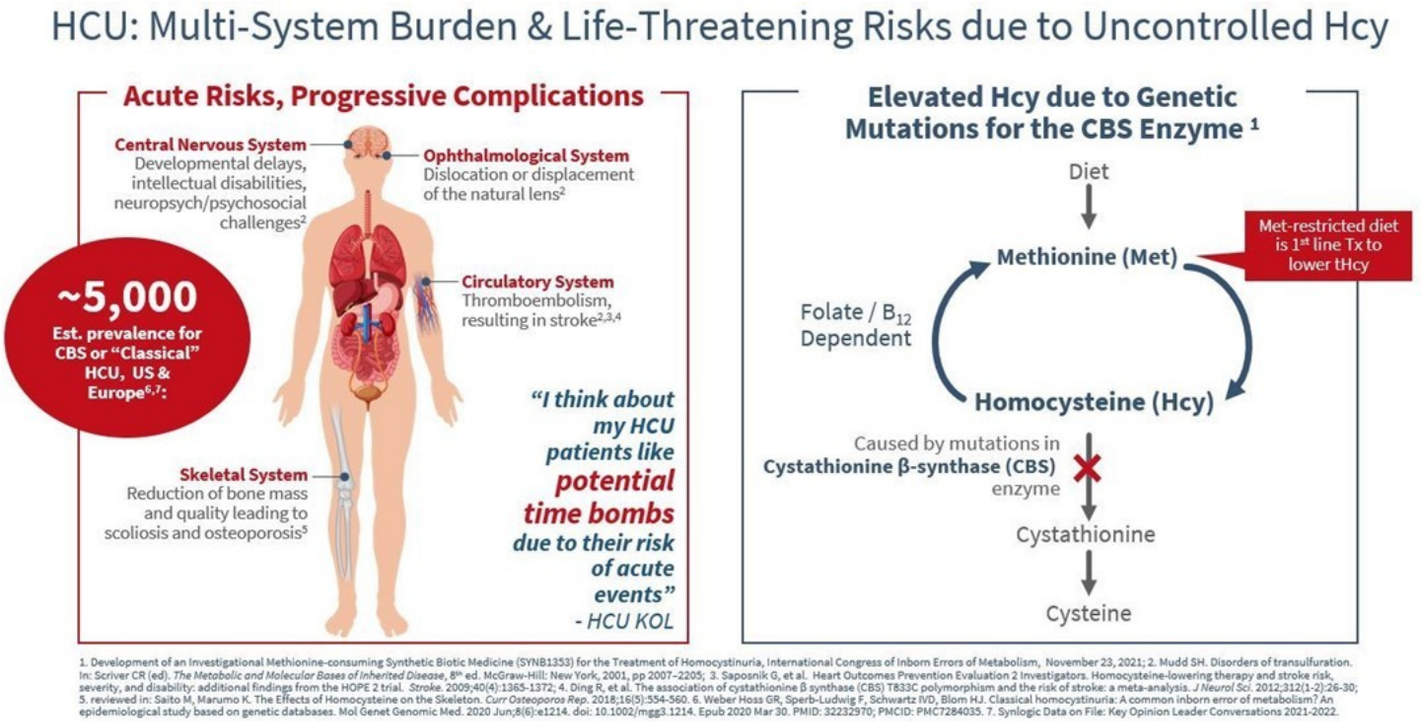
In November 2021 we announced the nomination of SYNB1353, a novel, orally administered, non-systemically absorbed drug candidate designed to lower plasma levels of homocysteine (Hcy) in patients with HCU by consuming methionine (Met), a precursor to Hcy. We also shared at that time that mechanistic modeling data suggests that SYNB1353 may lower plasma Hcy by up to 58% and may increase protein intake in HCU patients.

In November 2022, we announced that proof of mechanism was achieved with SYNB1353 through positive results in the Phase 1 study of healthy volunteers using a dietary model of HCU, in which we showed the translation from SYNB1353's activity in the GI tract to a lowering of plasma levels of Met. SYNB1353 has received Fast Track, Orphan Drug, and Rare Pediatric Disease Designations from the FDA as a potential treatment for HCU.

Science of HCU

HCU is a rare inherited metabolic disorder that affects the metabolism of the amino acid methionine (Met), a protein found in many foods including meat, fish, and dairy products. HCU is caused by a genetic defect which results in the absence of an enzyme known as cystathionine beta-synthase (CBS). When CBS is absent, Hcy and other toxic chemicals and their byproducts, including Met, build up in the blood and urine. In HCU, elevated total homocysteine (tHcy) levels are associated with a multisystem disorder, including impairments of the eye (ectopia lentis and/or severe myopia), skeletal system (excessive height, long limbs, scoliosis, pectus excavatum), vascular system (thromboembolism), and CNS (development delay and intellectual disability). The goal in treating HCU

is to reduce and control levels of tHcy, thereby reducing risk of acute, potentially life-threatening blood clots and chronic, multisystem complications.



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There is currently no cure for HCU and treatment options are limited. Patients must follow a rigid diet low in protein to avoid dietary Met intake. Other therapeutic approaches include vitamin supplements to minimize some of the disease side effects. Approximately 5,000 individuals in the United States and Europe suffer from CBS or "Classical" HCU.

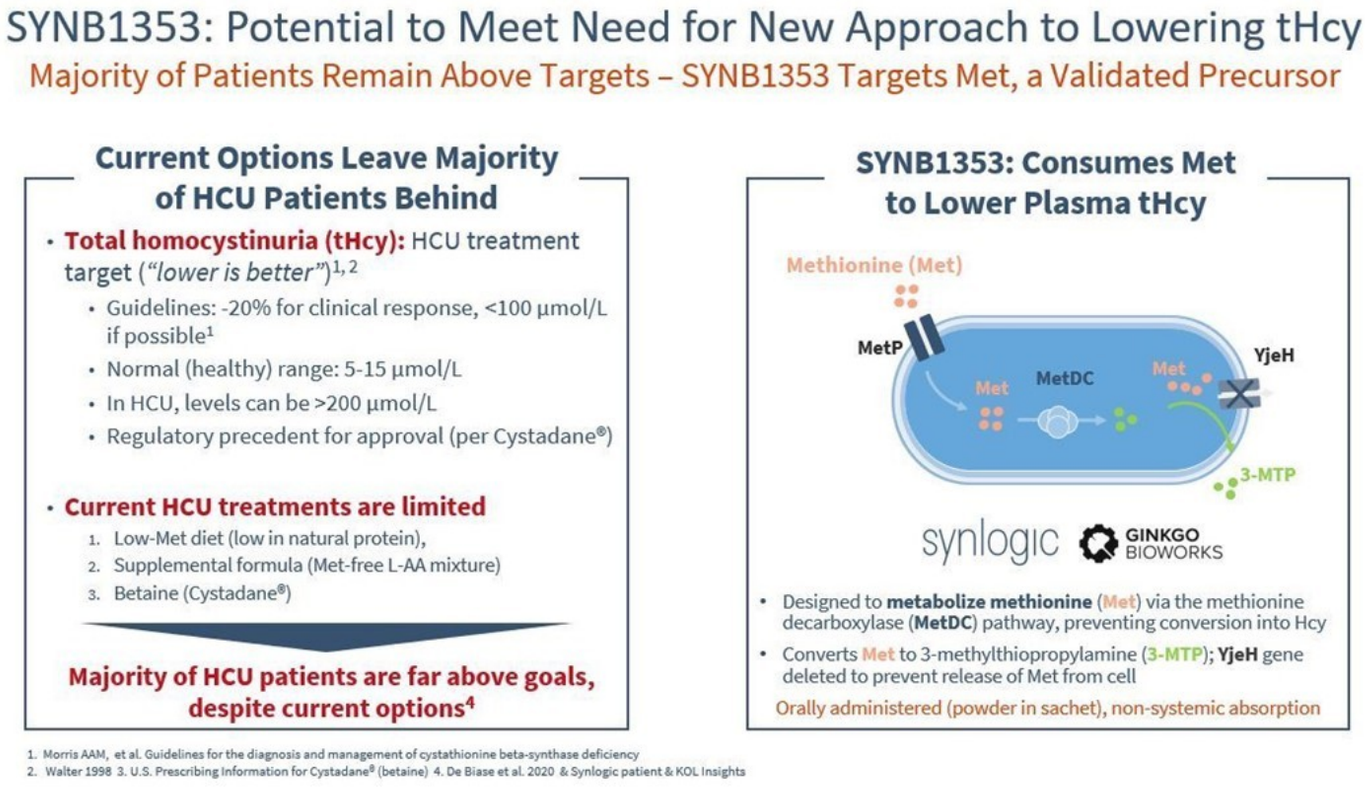
Limitations of Current HCU Treatments

Approved pharmacological treatment options for HCU are limited due to efficacy and tolerability. People with more mild phenotypes of HCU typically respond effectively to, and are sufficiently managed by, taking Vitamin B6 (also known as pyridoxine-responsive). Non-responders require a combination of betaine (brand name Cystadane®) and a moderate to severe dietary Met restriction. The severely protein-restricted diet is complex and challenging for long-term adherence. Compliance with treatment often deteriorates, particularly in adolescence, as in other disorders requiring dietary adherence. Patients report significant challenges with the burden of the low protein diet, intake of amino acid mixtures, and the palatability of protein substitutes as well as betaine. Reaching tHcy treatment targets remains a challenge despite existing pharmacotherapies.

SYNB1353 for HCU

A diet low in Met, a precursor to Hcy, is standard treatment for lowering tHcy levels in patients with HCU. This dietary model provided the scientific rationale for SYNB1353, which was engineered to produce an enzymatic pathway to metabolize Met, and thus lower plasma levels of tHcy. SYNB1353 metabolizes Met via the methionine decarboxylase (MetDC) enzymatic pathway, which prevents the conversion of Met into Hcy, thereby lowering tHcy in HCU patients and reducing risk of complications. SYNB1353 is taken as an orally administered, non-systemically absorbed live biotherapeutic drug candidate that, like our PKU drug candidates, is provided as a lyophilized powder in a sachet, to be orally administered with meals three times a day. We hold

worldwide development and commercialization rights to SYNB1353, which was developed as part of our research collaboration with Ginkgo.



In November 2022, we announced that proof of mechanism was achieved with SYNB1353 through positive results in the Phase 1 study of healthy volunteers using a dietary model of HCU. Top-line results demonstrated that SYNB1353 reduced in plasma Met when measured over 24 hours as area under the curve (AUC) following a Met meal challenge. SYNB1353 was generally well tolerated, and adverse events (AEs) were all mild to moderate, transient, and predominantly GI in nature. The frequency and severity of GI-related AEs were similar in the active and control group. During 2023, we conducted fermentation process improvements that successfully further increased activity of methionine degradation for SYNB1353.

Clinical Pipeline: Earlier-Stage Programs

Our Enteric Hyperoxaluria Program

SYNB8802 is a novel, orally administered, non-systemically absorbed drug candidate that was being developed for the treatment of enteric hyperoxaluria, a chronic, progressive disease characterized by high levels of urinary oxalate (Uox), a well-recognized cause of recurrent kidney stones.

Hyperoxaluria is a disease which results from excessive levels of oxalate in the body. Oxalate can be found naturally in the body or in foods with high oxalate levels such as leafy greens, potatoes, almonds, coffee, and beans. Humans do not have an inherent physiological need for oxalate and it is normally excreted through the kidney. Excessive levels of oxalate, when present in the urine, bind with calcium in the kidney and lead to nephrolithiasis (kidney stone formation), nephrocalcinosis, chronic kidney complications and renal disease.

Enteric hyperoxaluria often occurs as a result of a primary insult to the bowel, such as Crohn's disease, short bowel syndrome, or surgical procedures such as Roux-en-Y bariatric weight-loss surgery. This results in GI malabsorption, causing increased absorption of oxalate across the GI tract into the circulation. Oxalate crystals can damage kidneys, leading to chronic kidney disease and end-stage renal disease (ESRD). There are no approved treatments for enteric hyperoxaluria.

There is a direct link between elevated Uox and increased probability of kidney stone events or other renal adverse outcomes in patients with enteric hyperoxaluria. Even modest reductions in Uox can reduce the odds of developing a kidney stone. A recent epidemiological study conducted in 297 patients with enteric hyperoxaluria demonstrated that a 20% reduction in Uox resulted in as

much as a 25% reduction in the annual risk of having a kidney stone in the subsequent year in patients with recurrent kidney stones (D'Costa, Nephrol Dial Transplant 2020).

There are currently few approved treatments for primary hyperoxaluria, a rare genetic disease wherein the liver produces excessive levels of oxalate. Approved treatments for primary hyperoxaluria target the liver, and thus are not beneficial to patients with enteric hyperoxaluria, given its etiology is in GI malabsorption, and not hepatic over-production.

We estimate that there are 200,000 to 300,000 patients with recurrent kidney stones due to enteric hyperoxaluria in the United States. Existing treatment options are generally non-specific and include high fluid intake to increase urine output to more than two to three liters per day, a diet low in salt and oxalate, oral citrate and/or calcium and/or magnesium supplementation. We believe a clear need exists for therapies that lower dangerously high levels of Uox to reduce the risk of recurrent kidney stones in this patient population.

In May 2020, we announced the nomination of a clinical candidate for enteric hyperoxaluria, SYNB8802, which was designed using precision genetic engineering of *E. coli* Nissle to lower Uox levels by consuming oxalate throughout the GI tract through the addition of three different enzymes. In vivo studies in both mice and non-human primates demonstrated that SYNB8802 decreased Uox levels in an acute model of hyperoxaluria induced by dietary intervention. A detailed description of the engineering of SYNB8802 and data from these preclinical studies in an animal model of disease and healthy non-human primates was published in Molecular Systems Biology (Lubkowicz et al 2022). In 2021, we reported positive proof-of-mechanism for SYNB8802 from a Phase 1b study that demonstrated lowering of urinary and fecal oxalate levels in healthy volunteers with diet-induced hyperoxaluria, and in December 2022, we shared data confirming that SYNB8802 demonstrated proof of concept through clinically significant -38% lowering of Uox in a Phase 1b study in patients with a history of gastric bypass surgery.

Our Gout Program

SYNB2081 is designed to consume uric acid in the GI tract with the goal of lowering systemic uric acid levels as a potential treatment for gout, a complex form of inflammatory arthritis. Current treatment options present limitations in both safety and efficacy. SYNB2081 presents a novel, orally administered, non-systemically absorbed drug candidate created through our research collaboration with Ginkgo.

Gout occurs when excess uric acid in the body forms crystals in the joints. Patients can experience symptoms such as intense joint pain, inflammation and redness, and limited range of motion in the affected joints due to excessive levels of uric acid. In addition, gout is a recognized risk factor in chronic kidney disease. Due to present limitations in current treatment options, we believe that there is a clear need for a new approach.

In August 2022 we announced SYNB2081 as our drug candidate for the potential treatment of gout and the second product to advance to clinical development through our collaboration with Ginkgo.

Designing and Developing Synthetic Biotics

The Synthetic Biotics we design have unique advantages as potentially safe, effective, orally administered biotherapeutics. Engineered microbes can be programmed to carry out functions that cannot be performed by conventional drug treatments, such as small molecules or antibodies. Unlike other targeted approaches such as gene or RNA-targeted therapies, Synthetic Biotics are reversible, as they are engineered to be non-colonizing and are rapidly cleared via excretion. They have a reduced risk of adverse events due to the lack of systemic absorption.

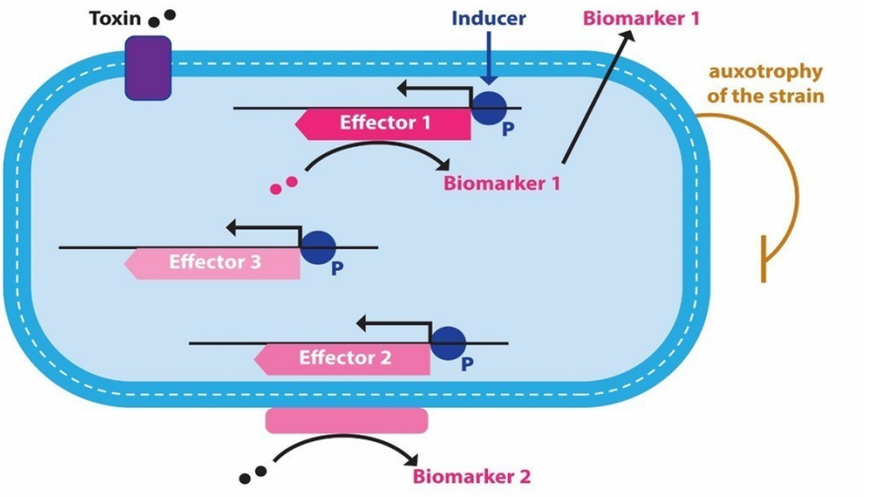
Using Synthetic Biology to Generate Synthetic Biotics

Bacteria have evolved over millions of years to adapt, survive, and actively metabolize to consume or produce metabolites in the human body. They are also amenable to genetic manipulation. To confer a therapeutic effect, we use basic biological properties of bacteria and the tools of synthetic biology to develop Synthetic Biotics from non-pathogenic microbes, focusing initially on a single strain of the bacteria *E. coli* Nissle.

Our scientists genetically engineer probiotic, non-pathogenic bacteria to create biological circuits to direct cellular processes in a manner analogous to designing electrical circuits. We aim to precisely and appropriately control the amount, location and activity of our Synthetic Biotics to address specific diseases and target biology of interest.

The critical parts of an engineered Synthetic Biotic medicine include (1) the chassis, or non-pathogenic bacterium (in our case *E. coli* Nissle), (2) the effector module(s), which is a gene or pathway encoding the core biological activity that provides the

therapeutic function, and (3) tunable switches that are designed to respond to specific disease states or environment signals to precisely control the activity, potency, and performance of the effector modules.



1. **The Chassis:** Our Synthetic Biotic platform starts with a well-characterized probiotic to serve as the chassis upon which we build our living medicines. Our research and development programs use *E. coli* Nissle, which is one of many non-pathogenic probiotics isolated from the human microbiota. *E. coli* Nissle is non-colonizing and has been used as a probiotic bacterial supplement for many 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 complete clearance from subjects in our Phase 1 clinical trial of SYNB1618 in healthy volunteers (Puurunen et al 2021 Nature Metabolism 3; 1125-1132). 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. There are several additional features of *E. coli* Nissle organism that makes it an attractive chassis for our platform:

    - *E. coli* Nissle's 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.
    - 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.
    - Starting from known principles of manufacturing helps de-risk Synlogic's proprietary large-scale manufacturing platform.
    - As a Gram-negative bacterium, with a protective outer wall, *E. coli* Nissle survives well in the human GI tract.

2. **The Effector Module or Circuit:** Synthetic Biotics have the advantage that they can be designed with multiple pathway components. We have engineered 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. Our approach allows us to engineer two types of mechanistic activities into our Synthetic Biotics: 1) we can engineer Synthetic Biotics capable of metabolic transformations that can substitute or compensate for missing or defective pathways in a patient, and 2) we can engineer Synthetic Biotics to produce therapeutically beneficial molecules.

    The enzymatic pathways needed to produce or convert molecules are protected from the harsh GI environment by their location within the cell cytoplasm of *E. coli* Nissle, allowing them the potential to function throughout the GI tract. We have leveraged proprietary tools, know-how and intellectual property to build multiple Synthetic Biotics that produce therapeutically relevant effects in pre-clinical experiments. Progression of these 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 control the activity of the genetic pathways we introduce into our Synthetic Biotics, with the goal of controlling the engineered circuit or its therapeutic output. To optimize the fitness and activity of a Synthetic Biotic, it is critical that the effector is activated at the appropriate time and

place to mediate its function. Switches are based on engineering DNA elements called "inducible promoters" that are designed to respond to disease states, specific environmental signals, or exogenously added inducing molecules.

Advantages of Synthetic Biotic Biotherapeutics

We believe our Synthetic Biotics will provide safe and effective therapies given the following attributes:

1. Synthetic Biotics Have Potential to Address Unmet Needs Not Possible with Other Modalities

Degrading Toxic Metabolites: Unlike other therapeutic approaches, Synthetic Biotics can be programmed with a unique mechanistic activity. For internal metabolic programs, we are engineering Synthetic Biotics with entire pathways designed to degrade or convert toxic metabolites. We believe that using a metabolizing pathway is advantageous compared to gene, RNA or enzyme replacement therapies because the latter are limited to targeting a single gene or protein defect and may require several unique drug products to address genetically heterogeneous patient populations. Compensating with an entire pathway delivered in bacteria Synthetic Biotics may provide a safe, therapeutic solution to broader disease populations as a single engineered therapeutic. Our clinical stage programs, SYNB1934, SYNB8802 and SYNB1353, are examples of Synthetic Biotics designed and engineered to eliminate metabolites from the GI tract and prevent their absorption.

Production of Therapeutic Molecules: Synthetic Biotics can also be programmed to produce beneficial molecules, such as bacterial metabolites that may improve disease or proteins that can be secreted from the bacteria into the local environment. Examples of this approach include production of short chain fatty acids (Reeves et al. DDW 2022), aryl hydrocarbon (AHR) agonists (Shu et al. DDW2022) and secretion of human IL-22 protein (Reeves et al. DDW 2022).

Combinations of Mechanisms: By incorporating multiple effectors or enzymes into a single strain, Synthetic Biotics have the potential to address multifactorial disease biology more effectively. For example, Synthetic Biotics can be engineered with multiple enzymes which convert toxic metabolites more effectively than a single effector could otherwise provide. Alternatively, pathways that degrade a metabolite of interest can be engineered into a Synthetic Biotic that also produces one or more therapeutic molecules.

2. Synthetic Biotics Have Potential to Reduce Safety Risks by Providing Local Therapeutic Delivery

We believe that when delivered locally, Synthetic Biotics have the potential to avoid the risks often associated with systemic therapies, especially when combinations of systemic therapies are required. Our Synthetic Biotic drug candidates are orally administered, and act locally while transiting through the gut. Consequently, they decrease toxic metabolite levels in the blood to provide a systemic therapeutic benefit to the patient. Given the potential for chronic oral dosing, Synthetic Biotics may have benefits in terms of dose prediction and reversibility of activity.

3. The Synthetic Biotic Approach is a Favorable Engine for Pharmacology

Features of our Synthetic Biotic product engine enable a highly efficient drug discovery and development with the potential of advancing clinical candidates more rapidly and efficiently than traditional approaches. Reasons for this include:

- *E. coli* Nissle chassis is used across programs. Because our lead programs are based on *E. coli* Nissle, experience can be leveraged broadly across the portfolio to further optimize the efficiency and reproducibility of discovery, development and manufacturing efforts. The non-colonizing nature of *E. coli* Nissle can be combined with engineering approaches to enhance 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. In addition, our chassis can be engineered to remove genes responsible for the production of the potential genotoxin colibactin, as an added safety features (Kalantari et al. Plos One 2023).
- Predictive pharmacology and biomarkers. Synthetic Biotic programs are designed to achieve a target activity and support 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 Biotics to drive optimization and decision-making. By assessing the activities of our Synthetic Biotic programs using 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 are further refined to inform dosing and development decisions for our additional programs.

- Stability and manufacturing. Starting from known principles of manufacturing helps de-risk Synlogic's proprietary large-scale manufacturing platform. 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 biomass generation while maintaining robust and cost-efficient scale up of product candidates.
- Manufacturing campaigns have demonstrated production reproducibility and robustness at multiple scales. The stability profile of our material has translated through the development and scale up efforts, supporting the shelf life of our strains. The implemented late stage and scale up capabilities have enabled us to produce 10,000 to 15,000 drug product doses at multiple strengths.

Collaboration Agreements

To accelerate the development and commercialization of Synthetic Biotics to patients, we have formed strategic alliances with collaborators that can expand our pipeline of therapeutic development and product candidates.

Roche

In June 2021, we entered into a Pilot Collaboration and Option Agreement (the Roche Collaboration and Option Agreement) with F. Hoffmann-La Roche Ltd (Roche Basel) and Hoffmann-La Roche Inc. (Roche US, and together with Roche Basel, Roche). Under the terms of the Roche Collaboration and Option Agreement, we and Roche sought to collaborate to research and pre-clinically develop Synthetic Biotics for addressing an undisclosed novel target for the treatment of inflammatory bowel disease.

Pursuant to the Roche Collaboration and Option Agreement, Roche agreed to pay us an upfront, nonrefundable technology access fee of $1.0 million, which we received in July 2021. In August 2022, the Company completed the research and development services for the second phase of the research plan and achieved a milestone payment of $1.5 million, which was paid by Roche in October 2022. In October 2023, the Company completed the research and development services for the third phase of the research plan and achieved a milestone payment of $2.5 million, which was paid by Roche in December 2023. The Roche Collaboration and Option Agreement concluded when Roche did not exercise its exclusive option to enter into a licensing and collaboration agreement for further development and commercialization of the product candidate.

Ginkgo Bioworks, Inc.

In June 2019, we entered into an agreement with Ginkgo. The agreement provided an $80 million equity investment at a premium in Synlogic by Ginkgo and entry into a long-term strategic platform collaboration to expand and accelerate the development of Synlogic's pipeline of Synthetic Biotics. We are using Ginkgo's cell programming platform to build and test thousands of microbial strains to accelerate progression of early preclinical leads to drug candidates optimized for further clinical development.

As part of the agreement, Ginkgo purchased 422,718 shares of our common stock and accompanying Pre-Funded Warrants (the Pre-Funded Warrants) to purchase up to 169,874 shares of our common stock, at a combined price of $135.00 per share and Pre-Funded Warrant. Gross proceeds were approximately $80 million. Under the agreement, we made a prepayment to Ginkgo of $30 million for its foundry services that are being provided to us over an initial term of five years, which can be extended. Upon the expiration of such initial term and, if applicable, such additional period, any portion of our prepayment that has not been used to purchase services from Ginkgo will be retained by Ginkgo. We have exclusive rights to any Synthetic Biotics that we develop as part of the collaboration and to intellectual property covering such products.

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 rely on additional regulatory protection afforded through orphan drug designations when applicable. 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; and
- 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. As of March 12, 2024, we had over 200 Synlogic-owned patents and patent applications in U.S. and foreign jurisdictions, of which over 75 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 , hyperphenylalaninemia, hyperoxaluria, homocystinuria, hyperuricemia, hyperammonemia, certain other inherited metabolic diseases and conditions, 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 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 engineered bacterial strain compositions, related formulations, methods of making the bacterial strains, methods of measuring strain activity, 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 patents and patent applications have expiration dates ranging from December 2035 to December 2044, depending on the indication and excluding any patent term adjustments or extensions.

Platform Technology Applications

In addition to disease-specific technology, Synlogic has also developed a number of technologies broadly applicable across the Synlogic platform. We rely on a combination of patent application and trade secrets to protect our platform intellectual property. Exemplary platform technologies include our unique upstream and downstream GMP manufacturing processes, bacterial chassis-related and genetic circuitry-related technological developments, including, for example, improvements in inducible gene regulation, control of bacterial cell growth, and systems for importing metabolites, as well as systems for prevention of production of potentially genotoxic metabolites. These platform technologies, and our intellectual property coverage thereof, are broadly applicable to our therapeutic Synthetic Biotics.

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 over 40 registered or allowed trademarks.

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 New Drug Application (NDA) process and a new biologic must be approved by the FDA through the Biologics License Application (BLA), process before such products may be legally marketed in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs and biologics 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 required preclinical (or nonclinical) laboratory tests, animal studies and formulation studies performed in accordance with Good Laboratory Practice (GLP) and other applicable regulations;
- Submission to the FDA of an investigational new drug application (IND) which must become effective before shipment of investigational product for human clinical trials may begin;
- Approval by an independent institutional review board (IRB) or ethics committee at each clinical trial site before each clinical trial may be initiated;

- Performance of adequate and well-controlled human clinical trials performed in accordance with applicable IND regulations, Good Clinical Practice (GCP), and other clinical-trial related regulations to evaluate the safety and efficacy of the investigational product for each proposed indication;
- Good Manufacturing Practice (GMP) to prepare a drug substance and drug product analyzed using validated analytical methods;
- 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 for marketing approval, including payment of application user fees;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the biologic is produced to assess compliance with current Good Manufacturing Practice (cGMP) regulations to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- Potential FDA audit of the clinical trial sites to assure compliance with GCP and the integrity of the clinical data submitted in support of the BLA; and
- FDA review and approval of the BLA, including satisfactory completion of an FDA advisory committee review of the product candidate, where appropriate or if applicable, prior to any commercial marketing or sale of the product in the United States.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry and formulation, animal toxicity and pharmacology studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P.L. 117-328) amended the FDCA and the Public Health Service Act to specify that nonclinical testing for drugs and biologics may, but is not required to, include in vivo animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various in vitro assays (e.g., cell-based assays, organ chips, or microphysiological systems), in silico studies (i.e., computer modeling), other human or nonhuman biology-based tests (e.g., bioprinting), or in vivo animal tests. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology 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 the topic at the time the guidance 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 INDs for our Synthetic Biotic product candidates. The sponsor will also include in the IND a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if a first phase study lends itself to an efficacy evaluation. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after an IND for an investigational product candidate is submitted to the FDA and human clinical trials have been initiated. 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, and 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 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 rules and regulations. Study subjects must sign the IRB-approved informed consent form in order to participate in the clinical trial.

In addition, an IRB representing each institution that is participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to clinical trial subjects. An IRB must operate in compliance with FDA 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 candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is usually 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 candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: Larger clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, often 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. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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.

In the Consolidated Appropriations Act for 2023, Congress amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. A sponsor must submit a diversity action plan to FDA by the time the sponsor submits the trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect Phase 3 trial planning and timing or what specific information FDA will expect in such plans, but if FDA objects to a sponsor's diversity action plan and requires the sponsor to amend the plan or take other actions, it may delay trial initiation.

The FDA or the sponsor may suspend or terminate 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 clinical protocol, cGMP or IRB requirements or if the product candidate 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 clinical testing may not be completed successfully within any specified period, if at all.

During the development of a new biologic, sponsors have the opportunity 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 with the FDA and to present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the investigational biologic. 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 the additional animal studies that may be required for approval and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing acceptable 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 product. 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 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. The annual report is customarily submitted in the form of a Development Safety Update Report (DSUR) which is accepted as being equivalent to an IND Annual Report and also meets requirements of the EU (European Union) and International Conference on Harmonization (ICH).

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of most clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at 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 submit the results of their clinical trials after completion, but disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and both NIH and FDA recently began enforcing those requirements against non-compliant clinical trial sponsors.

U.S. Review and Approval Processes

Assuming successful completion of the required clinical testing, the results of the nonclinical studies and clinical trials, along with detailed information relating to the product's chemistry, manufacturing, and controls, stability, quality control and product release procedures, proposed labeling, and other relevant information are submitted to the FDA as part of a BLA, requesting approval to market the product for one or more indications. The submission of a BLA is subject to the payment of a significant user fee (for example, for FY2024 this application fee exceeds $4 million); 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 sponsor of an approved BLA is also subject to an annual program fee, currently more than $415,000 per program. These fees are typically increased annually, but exemptions and waivers may be available under certain circumstances (such as a waiver for the first human drug application submitted by a qualifying small business and exemptions for orphan products).

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. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original BLAs, the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification and a sponsor's process to respond to such inquiries. Specifically, the review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving a BLA, the FDA will typically conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. These pre-approval inspections may cover all facilities associated with the BLA submission, including component manufacturing, finished product manufacturing, and control testing laboratories. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with GCP requirements and the integrity of the clinical data submitted to the FDA. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may, for example, determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the BLA.

The FDA may refer any BLA including applications for novel biologic candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval.

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. 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. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure, potent and effective and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued identity, strength, quality, potency and purity.

If a product receives regulatory approval, the approval is limited to the conditions of use (e.g., patient population, indication) described in the BLA, which could restrict the commercial value of the product. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, 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 REMS (Risk Evaluation and Mitigation Strategies), 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.

Under the Pediatric Research Equity Act (PREA), as amended, an initial BLA or certain supplements to a BLA for a novel product must contain data to assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirement. Unless otherwise required by regulation, PREA does not typically apply to any therapeutic product for an indication for which orphan designation has been granted. The Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in 2012, made permanent the PREA requirement that a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan (PSP), within sixty days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 clinical trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including trial objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials or other clinical development programs.

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 non-patent marketing exclusivity available in the United States, and, if granted, it provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or listed patents. This six-month exclusivity may be granted if an NDA/BLA sponsor submits clinical pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application for the same drug/biologic. The issuance of a written request does not require the sponsor to undertake the described clinical trials. To date, we have not received or requested any FDA 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 Biologics Price Competition and Innovation Act (BPCIA), amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. 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 can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

Under the BPCIA, a manufacturer may submit an abbreviated application for licensure of a biologic that is biosimilar to or interchangeable with an FDA-licensed reference biological product. This abbreviated approval pathway is intended to permit a biosimilar to come to market more quickly and less expensively than if a "full" BLA were submitted, by relying to some extent on the FDA's previous review and approval of the reference biologic to which the proposed product is similar.

Under the abbreviated approval pathway, 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.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed. If pediatric studies are performed and accepted by the FDA as responsive to a Written Request, the 12-year exclusivity period will be extended for an additional six months.

In addition, the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a supplement for the reference product for a subsequent application filed by the same sponsor or manufacturer of the reference product (or licensor, predecessor in interest or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength or for a modification to the structure of the biological product that does not result in a change in safety, purity or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

The BPCIA is complex and is still being interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

To date, the FDA has approved a number of biosimilars, and numerous biosimilars have been approved in Europe. The FDA has also issued several guidance documents outlining its approach to reviewing and approving biosimilars and interchangeable biosimilars.

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 defined as 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. The benefits of orphan drug designation include research and development tax credits and exemption from FDA prescription drug user fees. Orphan drug designation, however, does not convey any advantage in or shorten the duration of the regulatory review and approval process.

Generally, if a product that receives orphan designation receives the first FDA approval for the orphan indication, the product is entitled to orphan drug exclusivity, which means that for seven years, the FDA is prohibited from approving any other applications to market the same drug or biological product for the same indication, except in limited circumstances described further below. Orphan exclusivity does not block the approval of a different drug or biologic for the same rare disease or condition, nor does it block the approval of the same drug or biologic for different conditions. As a result, even if one of our product candidates receive orphan exclusivity, the FDA can still approve different drugs or biologics for use in treating the same indication or disease, which could create a more competitive market for us. Additionally, if a drug or biologic designated as an orphan product receives marketing approval for an indication broader than what was designated, it may not be entitled to orphan drug exclusivity.

Orphan exclusivity will not bar approval of another product with the same drug or biologic for the same condition under certain circumstances, including if a subsequent product with the same drug or biologic for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety or a major contribution to patient care, or if the company with orphan drug exclusivity cannot assure the availability of sufficient quantities of the drug or biologic to meet the needs of persons with the disease or condition for which the drug or biologic was designated. 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.

Recent court cases have challenged FDA's approach to determining the scope of orphan drug exclusivity; however, at this time the agency continues to apply its long-standing interpretation of the governing regulations and has stated that it does not plan to change any orphan drug implementing regulations.

In May 2023, the FDA granted labafenogene marselecobac Orphan Drug Designation. Additionally, in October 2017, the FDA granted SYNB1618 Orphan Drug designation for the treatment of PKU and in November 2022, the FDA granted SYNB1353 Orphan Drug designation for the treatment of HCU.

Fast Track, Breakthrough Therapy, Rare Pediatric Disease and Priority Review Designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include Fast Track designation, breakthrough therapy designation and priority review designation.

To be eligible for a Fast Track designation, the FDA must determine, from the request of a sponsor, based on preclinical studies, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast Track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA or BLA for a Fast Track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA. In addition, Fast Track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process.

In addition, with the enactment of FDASIA in 2012, Congress created a new regulatory program for product candidates designated by FDA as "breakthrough therapies" upon a request made by the IND sponsors. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs or biologics designated as breakthrough therapies are also eligible for accelerated approval of their respective marketing applications. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case- by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an original BLA or for an NDA for a new molecular entity from the date of filing.

Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case- by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an original BLA or for an NDA for a new molecular entity from the date of filing.

The FDA grants Rare Pediatric Disease Designation (RPDD) for serious and life-threatening diseases that primarily affect individuals from birth to 18 years old and fewer than 200,000 persons in the U.S. Under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" designation may qualify for a pediatric priority review voucher (pPRV) that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The Rare Pediatric Disease Priority Review Voucher program was reauthorized in the Creating Hope Reauthorization Act in December 2020, allowing a product that is designated as a product for a rare pediatric disease prior to October 1, 2024 to be eligible to receive a Priority Review Voucher upon approval of a qualifying NDA or BLA prior to October 1, 2026.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, Fast Track designation, breakthrough therapy designation and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

In July 2023, the FDA granted Fast Track designation for the use of labafenogene marselecobac for the treatment of PKU. In addition, in April 2018, the FDA granted Fast Track designation for the use of SYNB1618 for the treatment of PKU. In August 2022, the FDA granted Fast Track designation for the use of SYNB1353 for the treatment of HCU. In January of 2023, Synlogic announced the FDA's granting of RPDD for SYNB1353 for HCU and for SYNB1934 for PKU.

Accelerated Approval Pathway

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 from the FDA 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. The FDA may also grant accelerated approval for such a drug or biologic when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint, and the product may be subject to expedited withdrawal procedures. Drugs and biologics granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

As part of the Consolidated Appropriations Act for 2023, Congress provided FDA additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under the Act's amendments to the FDCA, FDA may require the sponsor of a product granted accelerated approval to have a confirmatory trial underway prior to approval. The sponsor must also submit progress reports on a confirmatory trial every six months until the trial is complete, and such reports are published on FDA's website. The amendments also give FDA the option of using expedited procedures to withdraw product approval if the sponsor's confirmatory trial fails to verify the claimed clinical benefits of the product.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with

the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting biologics for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or a BLA supplement, which may require the applicant to develop additional data or conduct additional pre-clinical studies and clinical trials. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. 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. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and finished product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. The manufacturing facilities for our product candidates must meet cGMP requirements and satisfy the FDA or comparable foreign regulatory authorities before any product is approved and our commercial products can be manufactured. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies and are subject to periodic prescheduled or unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our CMOs that may disrupt production or distribution or require substantial resources to correct. In addition, the discovery of conditions that violate these rules, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved BLA, including voluntary recall and regulatory sanctions as described below.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur or are discovered after the product reaches the market. Later discovery of previously unknown problems with a product may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs/BLAs or supplements to approved NDAs/BLAs, or suspension or revocation of product approvals;
- Product seizure or detention, or refusal to permit the import or export of products;
- Injunctions or the imposition of civil or criminal penalties; and
- Consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs; or mandated modification of promotional materials and labeling and the issuance of corrective information.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act, or DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States, including most biological products. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a ten-year period, which culminated in November 2023.

Most recently, the FDA announced a one-year stabilization period to November 2024, giving entities subject to the DSCSA additional time to finalize interoperable tracking systems and to ensure supply chain continuity.

From time to time, new 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 will be 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 the performance of clinical trials outside the United States and commercial sales and distribution of our products outside of the United States. Whether or not we obtain FDA approval for a product candidate, 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 between countries and jurisdictions and can involve additional testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

European Union drug development, review and approval

In the European Union, our product candidates also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls.

The new Clinical Trials Regulation, (EU) No 536/2014, which took effect on January 31, 2022, aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU clinical trial portal and database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting member state, whose assessment report is submitted for review by the sponsor and all other competent authorities of all European Union member states in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

As in the United States, similar requirements for posting clinical trial information are described in the European Union (EudraCT) website: https://eudract.ema.europa.eu.

To obtain a marketing authorization of a drug in the European Union, we may submit marketing authorization applications, or MAA, either under the so-called centralized or national authorization procedures.

Centralized procedure

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the European Medicines Agency (the EMA) that is valid in all EU member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, advanced-therapy medicines (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions and viral diseases. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view

of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

National authorization procedures

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.

Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU member state, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Under the above-described procedures, before granting the marketing authorization, the EMA or the competent authorities of the member states of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Conditional approval

In specific circumstances, EU legislation (Article 14(7) Regulation (EC) No 726/2004 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the risk-benefit balance of the product candidate is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Pediatric studies

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

European Union regulatory exclusivity

In the European Union, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product

when applying for a generic or biosimilar marketing authorization in the European Union during a period of eight years from the date on which the reference product was first authorized in the European Union. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

European Union orphan designation and exclusivity

The criteria for designating an orphan medicinal product in the European Union, are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity in the European Union may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- The second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- The applicant consents to a second orphan medicinal product application; or
- The applicant cannot supply enough orphan medicinal product.

PRIME designation

The EMA grants access to the Priority Medicines, or PRIME, program to investigational medicines for which it determines there to be preliminary clinical data available showing the potential to address an unmet medical need and bring a major therapeutic advantage to patients. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies, or CAT, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

United Kingdom Regulation

From January 1, 2021, European Union law no longer directly applies in the United Kingdom. The United Kingdom has adopted existing European Union medicines regulation as standalone United Kingdom legislation with some amendments to reflect procedural and other requirements with respect to marketing authorizations and other regulatory provisions.

The Medicines and Healthcare products Regulatory Agency, or MHRA is responsible for regulating the United Kingdom medicinal products market (Great Britain and Northern Ireland). In order to market medicines in the United Kingdom, manufacturers must hold a United Kingdom authorization. On January 1, 2021, all European Union marketing authorizations were converted to United Kingdom marketing authorizations subject to a manufacturer opt-out. The United Kingdom has introduced a separate UK-specific processes for regulatory submissions and medicinal product marketing authorization, and the MHRA guidance states that the United Kingdom will have the power to take into account marketing authorizations made under the European Union decentralized and mutual recognition procedures. On January 1, 2024, the MHRA launched the International Recognition Procedure, or IRP, which provides for an expedited authorization procedure for products that have received positive marketing authorization decisions from trusted partner agencies, such as the EMA or the FDA. There are two available routes for assessment and recognition under the IRP:

- Recognition Route A – 60 days from validation of submission
    - Application must be based on a Reference Regulatory, or RR, marketing authorization within the previous two years
    - Any significant differences from the quality dossier approved by the RR requires assessment under Recognition Route B
    - Evidence of GMP compliance for manufacturing sites should be provided with submission
    - None of the Recognition Route B criteria are met
- Recognition Route B - 110 days from validation of submission with one planned clock stop (up to 60 days) at day 70 to allow applicant to respond to issues identified during review
    - Application must be based on a RR marketing authorization within the previous ten years.
    - Criteria requiring Recognition Route B include, among other things:
        - The RR granted a conditional or exceptional circumstances marketing authorization
        - Additional manufacturing sites included in the application were not assessed by the RR or a manufacturing site is not GMP certified
        - There are substantial changes to the manufacturing process compared to the process approved by the RR
        - Certain product types (e.g., advanced therapy medicinal products, orphan medicines, over-the-counter medicines)
        - A Risk Management Plan was not assessed by the RR
        - The RR required one or more post-authorization safety studies for the product
        - A companion diagnostic is necessary for correct use of the product

United Kingdom medicines legislation is subject to future regulatory change under the Medicines and Medical Devices Act 2021. This act sets out a new framework for the adoption of medicines regulation.

Different rules will apply in Northern Ireland following implementation of the Northern Ireland Protocol. In Northern Ireland, European Union central marketing applications will continue to apply.

The Trade and Cooperation Agreement, which sets forth a framework for partnership between the European Union and the United Kingdom, became effective as of January 1, 2021. The Trade and Cooperation Agreement contains an Annex in relation to medicinal products with the objective of facilitating availability of medicines, promotion of public health and consumer protection in respect of medicinal products between the United Kingdom and the European Union. The Annex provides for mutual recognition of Good Manufacturing Practice (GMP) inspections and certificates, meaning that manufacturing facilities do not need to undergo duplicate inspections for the two markets. The Annex establishes a Working Group on Medicinal Products to deal with matters under the Trade and Cooperation Agreement, facilitate co-operation and for the carrying out of technical discussions. It is expected that further bilateral discussions will continue with respect to regulatory areas not the subject of the Trade and Cooperation Agreement, including pharmacovigilance. The Trade and Cooperation Agreement also does not include reciprocal arrangements for the recognition of batch testing certification. However, the United Kingdom has listed approved countries, including the EEA which will

enable United Kingdom importers and wholesales to recognize certain certification and regulatory standards. The European Commission has not adopted such recognition procedures.

It is expected that the establishment of a separate United Kingdom authorization system, albeit with transitional recognition procedures in the United Kingdom, will lead to additional regulatory costs. In addition, additional regulatory costs will be incurred with respect to the lack of mutual recognition of batch testing and related regulatory measures.

Rest of the world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from jurisdiction to jurisdiction. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Coverage, Pricing and Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party coverage and 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. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors often rely on Medicare coverage policy and payment limitations in setting their own reimbursement rates but also have their own methods to individually establish coverage and reimbursement policies. As a result, obtaining coverage and adequate reimbursement can be a time-consuming and costly process. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost effectiveness of our products. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development. 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 aged 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. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development. 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. Other member states allow companies to fix their own prices for drug products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. 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 and other countries do not follow price structures of the United States and generally prices tend to be significantly lower.

The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution (arbitrage between low-priced and high-priced member states) can further reduce prices. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Other U.S. Health Care Laws and Regulations

If our product candidates are approved in the United States, we will have to comply with various U.S. federal and state laws, rules and regulations pertaining to health care fraud and abuse, including anti-kickback laws and physician self-referral laws, rules and regulations. Violations of the fraud and abuse laws are punishable by criminal and civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, including Medicare and Medicaid. These laws include:

- The federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the AKS or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA or federal civil money penalties statute;

- The federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal health care programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payers if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- The federal transparency requirements under the Physician Payments Sunshine Act require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare, Medicaid or the Children's Health Insurance Program to report, on an annual basis, to the Centers for Medicare and Medicaid Services (CMS) information related to payments and other transfers of value to physicians, certain advanced non-physician health care practitioners, and teaching hospitals or to entities or individuals at the request of, or designated on behalf of, such physicians, non-physician health care practitioners, and teaching hospitals as well as certain ownership and investment interests held by physicians and their immediate family members; and

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving health care items or services reimbursed by nongovernmental third-party payors, including private insurers.

In November 2020, HHS finalized significant changes to the regulations implementing the Anti-Kickback Statute, as well as the Physician Self-Referral Law (Stark Law) and the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the healthcare industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants.

Finally, the majority of states also have statutes or regulations similar to the aforementioned federal laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of their exceptions and safe harbors, it is possible that business activities can be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry.

Ensuring that business arrangements with third parties comply with applicable healthcare laws and regulations is costly and time consuming. If business operations are found to be in violation of any of the laws described above or any other applicable governmental regulations a pharmaceutical manufacturer may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of its operations.

Health Care Reform in the US and Potential Changes to Health Care Laws

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, Congress must reauthorize the FDA's user fee programs every five years and often makes changes to those programs in addition to policy or procedural changes that may be negotiated between the FDA and industry stakeholders as part of this periodic reauthorization process. Congress most recently reauthorized the user fee programs in September 2022 but without any substantive policy changes. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

As previously mentioned, the primary trend in the U.S. health care industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other health care funding and applying new payment methodologies. For example, in March 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; 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; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Legislative and regulatory changes under the ACA are possible, but it is unknown what form any such changes or any law would take and how or whether it may affect the biopharmaceutical industry as a whole or Elicio's business in the future. Elicio expects that changes or additions to the ACA, the Medicare and Medicaid programs, and changes stemming from other health care reform measures, especially with regard to health care access, financing or other legislation in individual states, could have a material adverse effect on the health care industry in the United States.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Notably the Further Consolidated Appropriations Act for 2020 into law (P.L. 116-94), which became law on December 20, 2019 includes a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 (the CREATES Act). The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic and biosimilar product developers access to samples of brand products. Because generic and biosimilar product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic and biosimilar products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic or biosimilar product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic and biosimilar product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

More recently, in August 2022, President Biden signed into the law the Inflation Reduction Act of 2022, or the IRA. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of a drug or biological product covered by Medicare Parts B or D must pay a rebate to the federal government if the drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities and entered into the first set of agreements with pharmaceutical manufacturers to conduct price negotiations in October 2023. However, the IRA's impact on the pharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. Those lawsuits are currently ongoing.

In addition to the IRA's drug price negotiation provisions, President Biden's Executive Order 14087, issued in October 2022, called for the CMS innovation center to prepare and submit a report to the White House on potential payment and delivery modes that would complement to IRA, lower drug costs, and promote access to innovative drugs. In February 2023, CMS published its report which described three potential models focusing on affordability, accessibility and feasibility of implementation for further testing by the CMS Innovation Center. As of February 2024, the CMS Innovation Center continues to test the proposed models and has started to roll out plans for access model testing of certain product types (e.g., cell and gene therapies) by states and manufacturers.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in recent years, several states have formed prescription drug affordability boards (PDABs). Much like the IRA's drug price negotiation program, these PDABs have attempted to implement upper payment limits (UPLs) on drugs sold in their respective states in both public and commercial health plans. For example, in August 2023, Colorado's PDAB announced a list of five prescription drugs that would undergo an affordability review. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmacy benefit managers (PBMs) and other members of the health care and pharmaceutical supply chain, an important decision that appears to be leading to further and more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including biopharmaceutical developers like us. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be

included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that these and other health care reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of health care and containing or lowering the cost of health care. The implementation of cost containment measures or other health care reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

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. Our products are defined as Genetically Modified Organisms (GMO) or Genetically Modified Micro-organisms (GMM) and, dependent on their classification and containment, may be subject to regulation.

The United States does not have any federal legislation that is specific to genetically modified organisms. GMOs are regulated pursuant to health, safety, and environmental legislation governing conventional products. The U.S. approach to regulating GMOs is premised on the assumption that regulation should focus on the nature of the products, rather than the process in which they were produced.

The clinical development and marketing of GMM within the European Union, and elsewhere, falls under different regulations and practices in each country, which may involve approval by environmental or other regulatory bodies, as well as health authorities, and may establish the requirement for a risk assessment for the testing or authorization of the product.

Manufacturing

We have made significant investments in our manufacturing organization, including process development and cGMP production infrastructure to establish manufacturing processes designed to support production of clinical trial material. The manufacturing processes are designed to enable 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 built a fully integrated development and manufacturing organization with an internal process development group, quality group and manufacturing capabilities with the lease of cGMP cleanroom space in Waltham, Massachusetts. We currently work with an external contract manufacturing organizations (CMOs) for fill finish production of late-stage clinical trial material.

Clinical trial material for our Phase 1 study of SYNB1618 for PKU was manufactured by a CMO. These first clinical trials used a frozen liquid and solid formulation as the drug presentation. Since then, we have made additional investment in our formulation development that optimizes our production of solid dose formulations for our clinical programs. The powder for oral suspension formulation capability allows us to produce a more user-friendly presentation for clinical development and future commercial use. We are continuing to invest and investigate the utility of additional presentations for solid formulations of our Synthetic Biotics including capsules.

To enable the production of high levels of cells, or biomass, we can engineer our Synthetic Biotics 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 Biotics. 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. We continue to devote resources to process development and the generation of improved products.

As we progress in clinical development, we will need to increase our production scale to support late-stage clinical trials and commercial manufacturing. We are in the process of assessing CDMOs who meet our criteria to supply our late-stage clinical

development and commercial supply. We will compare the merits of working with one or more CDMOs who meet our criteria with the possibility of building cGMP manufacturing capacity and capabilities internally.

Competition

The biotechnology industry is extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in synthetic biology and metabolic engineering of 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. 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. Our competitors include other companies developing potential therapeutics for the same indications that we are pursuing for our drug candidates, regardless of modality.

Human Capital

As of March 12, 2024, we had 6 full-time employees. Of our full-time employees, 4 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.

Talent Acquisition and Retention

We recognize that our employees are essential to our success. To this end, we support business growth by seeking to attract and retain best-in-class talent. We use internal and external resources to recruit highly skilled candidates for open positions. We believe that we are able to attract and retain the talent that is required to meet our business goals.

Health, Safety and Wellness

We have always invested, and will continue to invest, in the health, safety, and wellness of our employees. We provide our employees with access to a variety of innovative, flexible, and convenient health and wellness programs. Program benefits are intended to provide protection and security, so employees can have peace of mind concerning events that may require time away from work or that may impact their financial well-being. We provide an Employee Assistance Program ("EAP") which provides consultation, referrals and resources to help employees and their household manage everyday life and work challenges. We also reimburse for fitness and other similar programs, as well as offer periodic health challenges to encourage health and well-being.

Diversity, Equity, and Inclusion

We believe a diverse workforce is critical to our success. Our mission is to value differences in races, ethnicities, religions, nationalities, genders, ages and sexual orientations, as well as education, skill sets and experience. We are focused on inclusive hiring practices, fair and equitable treatment, organizational flexibility and training and resources.

Training and Development

We believe in encouraging employees to be lifelong learners by providing ongoing learning and leadership training opportunities. While we strive to provide real-time recognition of employee performance, we have a formal annual review process not only to determine pay and equity adjustments tied to individual contributions, but to identify areas where employees may benefit from additional training and development opportunities.

Information About Our Executive Officers and Directors

The following persons were our executive officers and directors as of March 19, 2024:

Name	Position
Executive Officers	
Antoine Awad	Principal Executive Officer

Mary Beth Dooley	Head of Finance
Directors	
Peter Barrett, Ph.D.	Chairman of the Board of Directors, Partner at Atlas Venture
Michael Burgess, MB, CHB, Ph.D.	Interim Chief Medical Officer, Turnstone Biologics
Lisa Kelly-Croswell	SVP & Chief Human Resources Officer, Boston Medical Center Health System
Michael Heffernan	Chief Executive Officer, Avenge Bio, Inc.
Patricia Hurter, Ph.D.	Former Chief Executive Officer, Lyndra Therapeutics
Nick Leschly	Chief Executive Officer, 2seventybio, Inc.
Edward Mathers	General Partner at New Enterprise Associates
Richard P. Shea	Consulting CFO, Danforth Advisors

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. On December 22, 2021, IBDCo was merged with and into Synlogic Operating Company, Inc. and IBDCo ceased to exist as a separate entity.

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). On August 25, 2017, in connection with, and prior to the completion of the Merger, Mirna effected a 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, using an exchange ratio, 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 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 Annual Report on Form 10-K 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.

Summary of Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in this section below, that represent challenges that we face in connection with the successful implementation of our strategy. The occurrence of one or more of the events or circumstances described in more detail in the risk factors below, alone or in combination with other events or circumstances, may have an adverse effect on our business, cash flows, financial condition and results of operations. Such risks include, but are not limited to:

- Our business to date has been almost entirely dependent on the success of SYNB1934, and we have decided to discontinue further development of SYNB1934 and devote significant time and resources to identifying and evaluating strategic alternatives, which may not be successful.
- If we do not successfully consummate a strategic transaction, our board of directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.
- We are a 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 will require substantial additional funding, which may not be available on acceptable terms, or at all.
- 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 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.
- 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.
- Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and its financial condition and results of operations.
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.

- A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or geopolitical tensions, such as the armed conflict between Russia and Ukraine or the conflict in the Middle East, may materially and adversely affect our business and our financial results.
- Even if we obtain regulatory approval for a product candidate, we will remain subject to ongoing regulatory requirements.
- 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.
- 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.
- 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 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.
- Ethical, legal and social concerns about synthetic biology and genetic engineering could limit or prevent the use of our technologies and limit our revenues.
- We may not be successful in obtaining or maintaining necessary rights to Synthetic Biotics, product candidates and processes for our development pipeline through acquisitions and in-licenses.
- We may not have sufficient patent term protections for our product candidates to effectively protect our business.
- 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.
- Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.
- 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.
- We may be subject to claims challenging the inventorship of our patents and other intellectual property.
- We may not be able to protect our intellectual property rights throughout the world.
- We have historically relied on and may in the future 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 have historically relied on and may in the future 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 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.
- 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.
- 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.

- 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.
- If we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

Risks Related to Our Evaluation of Strategic Alternatives

Our business to date has been significantly dependent on the success of SYNB1934, and we have decided to discontinue further development of SYNB1934 and devote significant time and resources to identifying and evaluating strategic alternatives, which may not be successful.

To date, we have invested significant efforts and financial resources in the research and development of SYNB1934, which was our lead product candidate in clinical trials. In February 2024, we voluntarily halted Synpheny-3 based on results of an internal review in advance of an upcoming independent Data Monitoring Committee (DMC) assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. In February 2024, started to reduce operating expenses while we evaluate our strategic alternatives with a goal to enhance stockholder value, including the possibility of a merger or sale of the Company. There can be no assurance that our process to identify and evaluate potential strategic alternatives will result in any definitive offer to consummate a strategic transaction, or if made what the terms thereof will be or that any transaction will be approved or consummated. If any definitive offer to consummate a strategic transaction is received, there can be no assurance that a definitive agreement will be executed or that, if a definitive agreement is executed, the transaction will be consummated. In addition, there can be no assurance that any transaction, involving our company and/or assets, that is consummated would enhance shareholder value. There also can be no assurance that we will conduct further drug research or development activities in the future.

Any such strategic transaction may require us to incur non-recurring or other charges, may increase our near-and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher-than-expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of our company or any acquired businesses.

If we do not successfully consummate a strategic transaction, our board of directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that the process to identify a strategic transaction will result in a successfully consummated transaction. If no transaction is completed, our board of directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, ultimately, such liquidation, since the amount of cash available for distribution continues to decrease as we fund our operations while we evaluate our strategic alternatives. In addition, if our board of directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation of our company, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. Our commitments and contingent liabilities may include (i) obligations under our employment and related agreements with certain employees that provide for severance and other payments following a termination of employment occurring for various reasons, including a change in control of our company; (ii) potential litigation against us, and other various claims and legal actions arising in the ordinary course of business; and (iii) non-cancelable facility lease obligations. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation of our company. If a dissolution and liquidation

were pursued, our board of directors, in consultation with its advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up of our company.

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

We are a 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 biopharmaceutical company developing Synthetic Biotics and we have incurred significant operating losses since our inception. Our net loss was approximately $57.3 million and $66.1 million for the fiscal years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of approximately $414.3 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.

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 in synthetic biology 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 or we enter into third-party arrangements with collaborators. 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;
- Our ability to achieve milestones with our collaborators;
- Potential advantages that our competitors and potential competitors may have in securing funding or developing competing technologies or products;
- Our ability to obtain additional capital that may be necessary to expand our business; and
- Other macro-economic factors outside of our control.

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, general industry trends, macro-economic conditions, 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;
- Perspectives on synthetic biology and genetic engineering;
- Perspectives on the programs of competitors;
- Additions or departures of key personnel;
- Business disruptions caused by 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 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 February 2024, we voluntarily halted Synpheny-3 based on results of an internal review in advance of an upcoming independent Data Monitoring Committee (DMC) assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. 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.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and its financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank (SVB), was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (the FDIC) as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership and on May 1, 2023, First Republic Bank was swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC stated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediate liquidity may exceed the capacity of such program. There is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we review our banking relationships as we believe appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we

have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- loss of access to working capital sources;
- potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements; or
- termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition.

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. For example, in February 2024, we voluntarily halted Synpheny-3 based on results of an internal review in advance of an upcoming independent DMC assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. 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 raise additional capital or generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional nonclinical studies and/or clinical trials, the results obtained from such new formulation may not be consistent with previous results obtained, or the regulatory authorities may need to further review and approve our process before we can proceed. Clinical trial delays could also shorten any anticipated periods of patent exclusivity for our product candidates and may allow competitors to develop and bring products to market before we do which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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

The scientific discoveries that form the basis for our efforts to generate and develop our product candidates are relatively recent. The scientific evidence to support the feasibility of developing drugs based on our approach is both preliminary and limited. Synthetic Biotics represent a novel therapeutic modality and their successful development by us may require additional studies and efforts to optimize their therapeutic potential. Any product candidates that we develop may not demonstrate in patients the therapeutic properties ascribed to them in laboratory and other preclinical studies, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways. We have also not yet succeeded and may never succeed in demonstrating efficacy and safety for our current or any future product candidates in a pivotal clinical trial. 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. Additionally, the FDA or other regulatory authorities may lack experience in evaluating the safety and efficacy of novel product candidates based on synthetic biology, which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our product candidates.

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. 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. For example, in February 2024, we voluntarily halted Synpheny-3 based on results of an internal review in advance of an upcoming independent DMC assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability.

The clinical trial and manufacturing requirements of the FDA, the EMA 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 Biotics 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 EMA or national regulatory agencies may not be indicative of what the FDA, and vice versa, may require for approval and different or additional nonclinical 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 create Synthetic Biotics 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 may be required to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety of the product;
- 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 use 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.

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 May 2023, the FDA granted orphan drug designation to labafenogene

marselecobac (SYNB1934) 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 exclusivity 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 some 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 orphan 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, and obtain approval for such products, orphan product exclusivity 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. In addition, 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.

We may seek a Rare Pediatric Disease Designation, or RPDD, for one or more of our product candidates. However, a BLA for one or more of our product candidates may not meet the eligibility criteria for a priority review voucher upon approval.

In January 2023, labafenogene marselecobac received Rare Pediatric Drug Designation (RPDD) for phenylketonuria and in December 2022, SYNB1353 received RPDD for homocystinuria. With enactment of the Food and Drug Administration Safety and Innovation Act in 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For the purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. The FDA may determine that a BLA for one or more of our product candidates does not meet the eligibility criteria for a priority review voucher upon approval. Moreover, due to the current statutory authority for the RPDD and voucher program, the FDA may not award the voucher to sponsors of marketing applications unless either (i) the drug has received rare pediatric disease designation as of September 30, 2024, and is then approved by the FDA no later than September 30, 2026; or (ii) Congress reauthorizes the program. Even if legislation is enacted that extends the date by which approval of the rare pediatric disease-designated drug must obtain approval to receive a priority review voucher, we may not obtain approval by that date, and even if we do, we may not obtain a priority review voucher.

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, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory authority approval. 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. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. 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 healthy volunteers or patients suffering from the disease or condition the product candidate is intended to treat and who meet other eligibility criteria. The timing of our clinical trials depends on our ability to recruit eligible subjects to participate as well as the completion of required follow-up evaluations. Patients and healthy volunteers may be unwilling to participate in our clinical trials because of negative publicity from adverse events related to novel therapeutic approaches, competitive clinical trials for similar patient populations, the existence of current treatments or for other reasons including due to concerns posed by local or global health emergencies. 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, the clinical trial administration practices of the contract research organization (CRO), or clinical trial sites, labor shortages at the CRO or clinical trial sites, benefits and convenience of administration of the product candidate being studied, the patient referral practices of physicians, the amount of attention provided to our trial by clinical trial sites, our efforts and the CRO efforts, 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. 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.

Congress also recently amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug or biologic to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. For any future Phase 3 trials we plan to conduct, we must submit a diversity action plan to the FDA by the time we submit plans for such Phase 3, or pivotal study, protocol to the agency for review as part of an IND, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 trial for our product candidates or what specific information FDA will expect in such plans. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in final data.

From time to time, we may publicly disclose interim, top-line or preliminary data from our nonclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data that we previously published. As a result, top-line and preliminary data should be viewed with caution until final data are available. Adverse differences between interim data and final data could significantly harm our business prospects. For example, in February 2024, we voluntarily halted Synpheny-3 based on results of an internal review in advance of an upcoming independent DMC assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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 or internationally, 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;
- Loss of key employees; 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.

We or the third parties upon which we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or geopolitical tensions, such as the armed conflict, between Russia and Ukraine or the conflict in the Middle East, may materially and adversely affect our business and our financial results.

Over the past several years, COVID-19 has affected segments of the global economy and it may materially affect our operations again, including potentially significant interruption of our clinical trial activities. In addition, there could be a continuing effect of COVID-19 to the business at FDA or other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates. The COVID-19 pandemic, including surges in cases could also have a material adverse effect on our clinical trial operations in the United States and elsewhere, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography.

COVID-19 may also affect employees of third-party contract research organizations and contract manufacturing organizations located in affected geographies that we rely upon to carry out our clinical trials.

While the potential economic impact brought by and the duration of COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, potentially reducing our ability to access capital, which could in the future negatively affect our liquidity. Similarly, the current conflicts between Ukraine and Russia and in the Middle East have created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. In addition, we have previously announced our intention to open a clinical trial site in Israel and this could be impacted by the events in the Middle East. A recession or market correction resulting from the continued spread of COVID-19 or the geopolitical tensions in Russia and Ukraine and in the Middle East, could materially affect our business and the price of our common stock.

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

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain marketing approval for a novel therapeutic product from the FDA and other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, laws or regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for commercialization of any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain that approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- The FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- We may be unable to demonstrate to the satisfaction of the FDA or other comparable foreign regulatory authorities that our product candidates are safe, pure and potent or effective for their proposed indications;
- The results of clinical trials may not meet the level of statistical significance required by the FDA or other comparable foreign regulatory authorities in order to support approval;
- We may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- The FDA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- The data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA, to the FDA or other equivalent marketing authorization application submissions to obtain regulatory approval in the United States or elsewhere;
- Upon review of our clinical trial sites and data, the FDA or comparable foreign regulatory authorities may find our record keeping or the record keeping of our clinical trial sites or investigators to be inadequate;
- The FDA or other comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- The approval policies or regulations of the FDA or other comparable foreign regulatory authorities or the laws they enforce may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, financial condition and results of operations. The FDA and other comparable foreign regulatory authorities have substantial discretion in the approval process and determining when or whether to grant regulatory approval will be obtained for any of our product candidates, and whether to impose any conditions on such marketing approvals as described below. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or other comparable foreign regulatory authorities.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, if any, they may grant approval contingent on the performance of costly post-marketing clinical trials, or they may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate or with restrictive risk mitigation measures or warning language or contraindications that make the approved product more difficult or costly to commercialize. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

The regulatory landscape related to clinical trials in the European Union (EU) recently evolved. The EU Clinical Trials Regulation (CTR) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR introduced a centralized process and only requires the submission of a single application to all member states concerned the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal or CTIS. Once the CTA is approved, clinical study development may proceed. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, which the CTR replaced, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials, including those that are ongoing, will become subject to the provisions of the CTR. Compliance with the CTR requirements by us, our collaborators and third-party service providers, such as CROs, may impact our development plans.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects.

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. A drug or biologic 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 grant 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 have received Fast Track designation for three of our product candidates and may seek such designation for one or more of our other 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 Fast Track designation. We were awarded fFast tTrack designation for SYNB1618 (an earlier generation of SYNB1934labafenogene marselecobac) in April 2018, for labofenogene marselecobac in July 2023, and for SYNB1353 in August 2022. Fast track designation does not ensure that we will receive marketing approval for the product candidate or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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

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

Manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices (cGMP) regulations and corresponding foreign regulatory manufacturing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any 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 ensure compliance. If our original marketing approval for a product candidate were 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 untitled or 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.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of our current and future therapeutic product candidates in other jurisdictions.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable foreign regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our future products will also be subject to approval.

We may submit marketing applications in other countries in addition to the United States. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign marketing approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

The FDA and other comparable ex-U.S. regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

We may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable ex-U.S. regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable ex-U.S. regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from ex-U.S. clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of ex-U.S. data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to current GCP requirements; and (iii) the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including the adequacy of the patient population studied and statistical powering, must be met. Furthermore, even where the ex-U.S. study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many ex-U.S. regulatory authorities have similar approval requirements. In addition, such ex-U.S. trials would be subject to the applicable local laws of the ex-U.S. jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable ex-U.S.

regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any comparable ex-U.S. regulatory authority does not accept such data, it would result in the need for additional trials.

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, increases in workload, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In 2023, for example, members of Congress wrote to officials at the FDA expressing their concern that clinical holds should not be a means for FDA to gain additional time to review a clinical protocol. 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. The coronavirus pandemic has also adversely affected the operations of necessary government agencies. 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, 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. In addition, competing demands from other companies or issues can affect the timeliness for which the FDA can review and process our regulatory submissions.

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

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA"), was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs and biologics, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased from 50% pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs and biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs or biologics to be covered under Medicare Part D.

Further legislative and regulatory changes under the ACA remain possible, although it is unknown what form any such changes or any law would take, and how or whether it may affect the biopharmaceutical industry as a whole or our business in the future. We expect that changes or additions to the ACA, the Medicare and Medicaid programs, such as changes allowing the federal government to directly negotiate drug prices, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry in the United States.

Further, over the past several years there has been heightened governmental scrutiny over the manner in which biopharmaceutical manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. The probability of success of these newly announced policies, many of which have been subjected to legal challenge in the federal court system, and their potential impact on the U.S. prescription drug marketplace is unknown. There are likely to be continued political and legal challenges associated with implementing these reforms as they are currently envisioned.

Most recently, in August 2022, President Biden signed into the law the Inflation Reduction Act of 2022, or the IRA. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of a drug or biological product covered by Medicare Parts B or D must pay a rebate to the federal government if the product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume

of a drug product that is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. Additional state and federal healthcare reform measures are expected to be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for certain biopharmaceutical products or additional pricing pressures.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, California requires pharmaceutical manufacturers to notify certain purchasers, including health insurers and government health plans at least 60 days before any scheduled increase in the wholesale acquisition cost (WAC), of their product if the increase exceeds 16%, and further requires pharmaceutical manufacturers to explain whether a change or improvement in the product necessitates such an increase. Similarly, Vermont requires pharmaceutical manufacturers to disclose price information on certain prescription drugs, and to provide notification to the state if introducing a new drug with a WAC in excess of the Medicare Part D specialty drug threshold. In addition, in the last few years, several states have formed prescription drug affordability boards (PDABs) with the authority to implement upper payment limits (UPLs) on drugs sold in their respective jurisdictions. However, there are several pending federal lawsuits challenging the authority of states to impose UPLs.

In December 2020, the U.S. Supreme Court also held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers, or PBMs, and other members of the healthcare and pharmaceutical supply chain, an important decision that appears to be leading to further and more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including biopharmaceutical developers like us. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or EU member state level may result in significant additional requirements or obstacles that may increase our operating costs.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action. We expect that additional federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

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 payments 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 government payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- 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 payments sunshine requirements under the ACA require manufacturers of drugs, devices, biologics, and medical supplies to report annually to CMS information related to payments and other transfers of value to physicians, certain advanced non-physician healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members; 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 healthcare reform legislation has strengthened these laws. For example, the ACA, among other things, amended 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 U.S. 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 healthcare 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 international 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 domestic and international laws and regulations governing data privacy, data security, and the protection of health-related and other personal information. The regulatory framework for collecting, using, safeguarding, sharing, transferring and other processing of personal information worldwide is rapidly evolving and in recent years there has been an increasing focus on privacy and data security issues with the potential to affect our business.

In the U.S., numerous federal and state laws and regulations, including state data breach notification laws, and federal and state consumer protection laws govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations, where applicable, could result in government enforcement actions, which could include civil or criminal penalties, private litigation and/or adverse publicity and could negatively affect our operating results and business. For example, California enacted the California Consumer Privacy Act (the CCPA), which took effect on January 1, 2020, and gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, in 2020, California voters passed the California Privacy Rights Act (the CPRA), which became effective as of January 1, 2023. The CPRA significantly amends the CCPA and imposes additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new regulatory entity, the California Privacy Protection Agency, which is authorized to issue substantive regulations under the CPRA and could result in increased privacy and information security enforcement. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the CPRA may increase our compliance costs and potential liability. In addition to California, more U.S. states are enacting similar legislation, increasing compliance complexity and increasing risks of failures to

comply. In 2023, comprehensive privacy laws in Virginia, Colorado, Connecticut, and Utah all took effect, and laws in Montana, Oregon, and Texas will take effect in 2024. In addition, laws in other U.S. states are set to take effect beyond 2024, and additional U.S. states have proposals under consideration, all of which are likely to increase our regulatory compliance costs and risks, exposure to regulatory enforcement action and other liabilities.

Additionally, the collection, use, disclosure, transfer, or other processing of personal data in the European Union, including personal health data, is subject to the General Data Protection Regulation, or GDPR, which took effect in 2018 and applies to companies within and outside of the European Union. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third-party processors in connection with the processing of the personal data. The GDPR also enhances enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the infringer, whichever is greater. Additionally, the GDPR confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the withdrawal of the United Kingdom from the European Union and the subsequent separation of the data protection regimes of these territories mean we are required to also comply with similar data protection laws in the United Kingdom, which may lead to additional compliance costs and could increase our overall risk.

Laws in the European Economic Area (EEA), Switzerland, and the UK on data export are also evolving. For example, the GDPR only permits exports of data outside the EU where there is a suitable data transfer solution in place to safeguard personal data (e.g. the EU Commission approved Standard Contractual Clauses or certification under the recently-adopted Data Privacy Framework). If we have to rely on third parties to carry out services for us, including processing personal data on our behalf, we are required under GDPR and similar laws in Switzerland and the UK to enter into contractual arrangements to help ensure that these third parties only process such data according to our instructions and have sufficient security measures in place. Any security breach or non-compliance with our contractual terms or breach of applicable law by such third parties could result in enforcement actions, litigation, fines and penalties or adverse publicity and could cause customers to lose trust in us, which would have an adverse impact on our reputation and business. Future actions of EU, Swiss, and UK data protection authorities are difficult to predict. Some customers or other may respond to these evolving laws and regulations by asking us to make certain privacy or data-related contractual commitments that we are unable or unwilling to make. This could lead to the loss of current or prospective customers or other business relationships.

Numerous international, 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 international 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 $50,000 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.

Other states have implemented similar laws protecting identifiable health and personal information, and most such laws differ from each other in significant ways and may not be preempted by HIPAA, thus complicating compliance efforts.

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.

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. Despite our efforts, we may not have fully complied in the past and may not in the future. 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.

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 cybersecurity incidents, which could result in a material disruption of our product development programs.

Our internal information technology, or IT, systems and those of our current and any future collaborators and other contractors, consultants, or clinical trial sites are vulnerable to damage from cyberattacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include the deployment of harmful malware,

ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering, phishing and other means to affect service reliability and threaten the confidentiality, integrity and availability of information and IT systems. If any of the above events 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 cybersecurity incident 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. The market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have processes to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies evolve and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. In addition, there can be no assurance that we will promptly detect any such disruption or cybersecurity incident, if at all. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal IT systems or those of our third-party contractors, or our consultants' efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, cybersecurity incident, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm, as well as loss of competitive advantage or loss of consumer confidence.

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 Biotics, delays or other impediments to our programs or the public acceptance and commercialization of Synthetic Biotics. Further, there is a risk that Synthetic Biotics 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 Biotics, 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.

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 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 being issued 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 or collaborators, 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 is 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. and foreign 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.

European patent practice is expected to change now that the European Unitary Patent (UP) and Unified Patent Court (UPC) went into force on June 1, 2023. The new system will impact both pending European applications and granted European patents, and uncertainty remains about long-term implications of this change. The UPC may particularly present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While the UPC is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. We will have the right to opt our patents out of the UPC system over the first seven years, but doing so may preclude us from realizing the benefits of the new unified court.

Obtaining And Maintaining Our Patent Protection Depends on Compliance with Various Procedural, Document Submission, Fee Payment and Other Requirements Imposed by Governmental Patent Agencies, And Our Patent Protection Could be Reduced or Eliminated for Non-Compliance with These Requirements.

Periodic maintenance fees on any issued patents are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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 biology. We may become 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 and we may in the future pursue available proceedings in the U.S. and foreign patent offices to challenge the validity of such 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 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 may 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.

Additionally, Europe's Unified Patent Court (UPC) may present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. Although this new court has been implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally challenge our patents if opted into the UPC, rather than having to seek invalidity or non-infringement decisions on a country-by-country basis. It will be several years before the scope of patent rights that will be recognized and the strength of patent remedies that will be provided is known.

Some of our intellectual property may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies if it is determined that our intellectual property has been discovered through government-funded programs. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have acquired or licensed or may acquire or license in the future may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental

purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products relating to such intellectual property. To the extent any of our future intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

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 have historically relied on and may in the future 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 have historically relied on and may in the future rely upon third parties, including independent clinical investigators, contracted laboratories and third-party CROs, to conduct our preclinical studies and clinical trials, as well as certain product candidate discovery and development activities, in accordance with applicable regulatory requirements and to monitor and manage data for our ongoing preclinical and clinical programs. We have historically relied on and may in the future rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and any third-party contractors and CROs we engage will be required to comply with GLP, as applicable, and GCP requirements, which are regulations and guidelines enforced by the FDA, the EMA and other comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GLP and GCP through periodic inspections of laboratories conducting GLP studies, and clinical trial sponsors, principal investigators, CROs, and trial sites when auditing for GCP compliance. If we, our investigators or any of our CROs or contracted laboratories that we engage fail to comply with applicable GLP and GCP, as applicable, the data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, the EMA or other comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications for our therapeutic product candidates. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our preclinical studies or clinical trials comply with applicable GLP or GCP regulations. In addition, our clinical trials must be conducted with product produced in compliance with applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat preclinical studies or clinical trials, which would delay the regulatory approval process.

Further, these laboratories, investigators and CROs are not our employees, and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent laboratories, investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their

performance is substandard, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

There is a limited number of third-party service providers that specialize or have the expertise required to achieve our business objectives. If any of our relationships with these third-party laboratories, CROs or clinical investigators terminate, we may not be able to enter into arrangements with alternative laboratories, CROs or investigators or to do so in a timely manner or on commercially reasonable terms. If laboratories, CROs or clinical investigators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols, regulatory requirements or for other reasons, our preclinical studies or clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

Switching or adding additional laboratories or CROs (or investigators) involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new laboratory or CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our contracted laboratories and CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and results of operations.

In addition, clinical investigators may serve as scientific advisors or consultants to us from time to time and may receive cash compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the preclinical study or clinical trial, the integrity of the data generated at the applicable preclinical study or clinical trial site may be questioned and the utility of the preclinical study or clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA. Any such delay or rejection could prevent us from commercializing our clinical-stage product candidate or any future therapeutic product candidates it may develop.

We have historically relied on and may in the future 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 have historically relied on and may in the future rely on third-party supply and manufacturing partners to supply the materials and components to manufacture parts of the process of 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, effective, or in an amount that satisfies our commercial needs.

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 Biotics 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 cGMP regulations. Although our agreements with our suppliers and manufacturers require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we have limited control over their conduct to implement and maintain these standards. 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 and may be required to conduct bridging studies or repeat clinical trials to assure comparable safety, purity and potency. 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.

In addition, our suppliers and manufacturers are subject to inspection and approval by regulatory authorities before we can commence the manufacture and sale of any of our product candidates, and thereafter are subject to ongoing inspection from time to time. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Any such failure by us or any of our suppliers or manufacturers would significantly impact our ability to develop, obtain regulatory approval for or, if approved, market our product candidates.

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 typically 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.

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, the macro-economic conditions may disfavor a collaboration, 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.

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. 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. Further there are several companies working to develop other similar products. 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 substantially greater 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.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we have historically focused and may in the future focus on research programs, therapeutic platforms and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

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 healthcare 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 healthcare 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.

The success of our business is expected to depend largely 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 CMS, an agency within DHHS, 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. No uniform policy for coverage and reimbursement for drug products exist among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic/biosimilar drug or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidate and other therapies as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidate over other available and comparable products, pricing of existing drugs may limit the amount we will be able to charge for its product candidate. These payors may deny or revoke the reimbursement status of a given drug product or establish prices for new or existing marketed products at levels that are too low to enable it to realize an appropriate return on our investment in product development. If coverage and reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on products that we may develop.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. For example, under these circumstances, physicians may limit how much or under what circumstances they will prescribe or administer our products and patients may deliver to purchase such products. This, in turn, could affect our ability to commercialize our products successfully and impact our profitability, results of operations, financial condition, and future success.

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. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. 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 on prescription drugs, has increased 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.

Our future product candidates for which we obtain approval may face competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate ahead of our competitors, our product candidates may face competition from biosimilar products. In the United States, Synthetic Biotic products are expected to be regulated by the FDA as biological products and we intend to seek approval for these product candidates pursuant to the BLA pathway. The BPCIA created an abbreviated pathway for FDA approval of biosimilar and interchangeable biological products based on a previously licensed reference product. Under the BPCIA, an application for a biosimilar biological product cannot be approved by the FDA until 12 years after the original reference biological product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity available to reference biological products. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference biological products pursuant to its interpretation of the exclusivity provisions of the BPCIA for competing products, potentially creating the opportunity for generic follow-on biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing including whether a future competitor seeks an interchangeability designation for a biosimilar of one of our products. Under the BPCIA as well as state pharmacy laws, only interchangeable biosimilar products are considered substitutable for the reference biological product without the intervention of the healthcare provider who prescribed the original biological product. However, as with all prescribing decisions made in the context of a patient-provider relationship and a patient's specific medical needs, healthcare providers are not restricted from prescribing biosimilar products in an off-label manner. In addition, a competitor could decide to forego the abbreviated approval pathway available for biosimilar products and to submit a full BLA for product licensure after completing its own preclinical studies and clinical trials. In such a situation, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its biological product as soon as it is approved.

Furthermore, the CREATES Act established a private cause of action that permits a follow-on product developer to sue the brand manufacturer to compel it to furnish necessary samples of a reference product on "commercially reasonable, market-based terms." If follow-on product developers request samples of any product candidates for which we receive marketing approval in order to conduct comparative testing to support one or more applications for a follow-on version of our products, and we refuse any such request, we may be subject to litigation under the CREATES Act. Although lawsuits have been filed under the CREATES Act since its enactment, those lawsuits have settled privately; therefore, to date, no federal court has reviewed or opined on the statutory language and there continues to be uncertainty regarding the scope and application of the law.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our product candidates, if approved, our future products may become subject to competition from such biosimilars, whether or not they are designated as interchangeable, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received 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 ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. 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. Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

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 12, 2024, our executive officers and directors, together with holders of 5% or more of our common stock outstanding and their respective affiliates, beneficially own the majority 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.

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 12, 2024, there were a total of 11,646,977 shares of our common stock outstanding. We have also registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and vesting provisions, as applicable.

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.

In addition, our amended and restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, or the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

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.

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.

We will continue to incur costs as a result of being a public company, and our management will continue to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, we expect that these rules and regulations will continue to make it more difficult and more expensive for us to maintain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in future uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

Our common stock is currently listed on the Nasdaq Capital Market and was previously listed on the Nasdaq Global Market. To maintain the listing of our common stock on the Nasdaq Global Market, we were required to satisfy minimum financial and other continued listing requirements and standards, including those related to the price of our common stock. On December 6, 2022, we received a written notice from the Listing Qualifications Department of the Nasdaq Stock Market (Nasdaq) notifying us that, based on the closing bid price of our common stock being below $1.00 per share for 30 consecutive business days, we no longer complied with Nasdaq's minimum bid price requirement in Listing Rule 5450(a)(1) for continued listing on the Nasdaq Global Market.

Pursuant to Nasdaq Listing Rule 5810(c)(3)(A), we were provided an initial compliance period of 180 calendar days from receipt of the Notice, or until June 5, 2023, to regain compliance with the minimum bid price requirement. To regain compliance, the bid price for our common stock would need to close at $1.00 per share or more for a minimum of 10 consecutive business days during this 180-day grace period, among other requirements.

On May 25, 2023, we submitted to the Listing Qualifications Department of Nasdaq an application to transfer the listing of our common stock from The Nasdaq Global Market to The Nasdaq Capital Market. On June 6, 2023, we received a notice (Extension Notice) from the Listing Qualifications Department informing us that Nasdaq granted us an additional 180 calendar days, or until December 4, 2023 to regain compliance with the minimum closing bid price requirement for continued listing on The Nasdaq Capital Market under Nasdaq Marketplace Rule 5550(a)(2). In connection with the Extension Notice, the listing of our common stock was transferred from the Nasdaq Global Market to the Nasdaq Capital Market, effective as of June 7, 2023. The Extension Notice had no other immediate effect on the listing of our common stock.

On September 27, 2023, we implemented a reverse stock split of our shares of common stock, pursuant to which every fifteen (15) shares of our issued and outstanding common stock was automatically converted into one (1) issued and outstanding share of

common stock without any change in the par value of $0.001 per share. The reverse stock split was approved by our stockholders on September 21, 2023 at our Special Meeting of stockholders.

On October 13, 2023, we received a written notice from the Listing Qualifications Department of Nasdaq notifying us that we had regained compliance with Listing Rule 5550(a)(2) and that this matter was closed. However, there can be no assurance that we will comply with the minimum bid price requirement in the future nor, is there any assurance that our common stock would never be delisted from Nasdaq at some future date. If our common stock were to be delisted from Nasdaq and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. Also, it may be difficult for us to raise additional capital if we are not listed on a major exchange.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

We recognize the critical importance of maintaining the trust and confidence of patients, business partners and employees toward our business and are committed to protecting the confidentiality, integrity and availability of our business operations and systems. Our board of directors is actively involved in oversight of our risk management activities, and cybersecurity represents an important element of our overall approach to risk management. In general, we seek to address cybersecurity risks through a cross-functional approach that is focused on preserving the confidentiality, security and availability of the information that we collect and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity incidents when they occur.

Cybersecurity Risk Management and Strategy; Effect of Risk

We face risks related to cybersecurity such as unauthorized access, cybersecurity attacks and other security incidents, including as perpetrated by hackers and unintentional damage or disruption to hardware and software systems, loss of data, and misappropriation of confidential information. To identify and assess material risks from cybersecurity threats, we maintain a comprehensive cybersecurity program and work with a third party managed service provider to ensure our systems are effective and prepared for information security risks, including regular oversight of our programs for security monitoring for internal and external threats to ensure the confidentiality and integrity of our information assets. We consider risks from cybersecurity threats alongside other company risks as part of our overall risk assessment process. We and our third-party partners employ a range of tools and services, including regular network and endpoint monitoring and protection, audits, vulnerability assessments, and penetration testing, to inform our risk identification and assessment. As discussed in more detail under “Cybersecurity Governance” below, our audit committee provides oversight of our cybersecurity risk management and strategy processes, which are led by our Chief Operating Officer.

We also identify our cybersecurity threat risks by using the services of a managed services provider. To provide for the availability of critical data and systems, maintain regulatory compliance, manage our material risks from cybersecurity threats, and protect against and respond to cybersecurity incidents, we undertake the following activities:

- monitor as appropriate emerging data protection laws and industry literature and implement changes to our processes that are designed to comply with such laws if needed;
- through our policies, practices and contracts (as applicable), require employees, as well as third parties that provide services on our behalf, to treat confidential information and data with care;
- employ technical safeguards that are designed to protect our information systems from cybersecurity threats, including redundant firewalls, intrusion prevention and detection systems, multi-factor authentication, encryption, anti-malware functionality and access controls;
- provide annual and routine mandatory training utilizing Knowbe4 (leading security awareness training module) for our employees and contractors regarding cybersecurity threats as a means to equip them with effective tools to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices;
- conduct phishing email simulations for employees and contractors with access to our email systems to enhance awareness and responsiveness to possible threats;

- utilize a managed services provider to help us identify, protect, detect, respond and recover when there is an actual or potential cybersecurity incident; and
- carry information security risk insurance that provides protection against the potential losses arising from a cybersecurity incident

Our incident response plan coordinates the activities we, in concert with our third party managed services provider, take to prepare for, detect, respond to and recover from cybersecurity incidents, which include processes to triage, assess severity for, escalate, contain, investigate and remediate the incident, as well as to comply with potentially applicable legal obligations and mitigate damage to our business and reputation.

Our processes also address cybersecurity threat risks associated with our use of third-party service providers, including our suppliers and manufacturers or who have access to patient and employee data or our systems. In addition, cybersecurity considerations affect the selection and oversight of our third-party service providers. We perform diligence on third parties that have access to our systems, data or facilities that house such systems or data, including through vendor security questionnaires as appropriate.

We describe whether and how risks from identified cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition, under the heading *"Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer cybersecurity incidents, which could result in a material disruption of our product development programs,"* which disclosures are incorporated by reference herein. In the last three fiscal years, we have not experienced any material cybersecurity incidents.

Cybersecurity Governance; Management

Cybersecurity is an important part of our risk management processes and an area of focus for our board of directors and management. Our board of directors executes its oversight responsibility for risk management both directly and through delegating oversight of certain of these risks to its committees, and our board of directors has authorized our audit committee to oversee risks from cybersecurity threats.

At least annually and on a periodic basis, our audit committee receives an update from management on our cybersecurity threat risk management and strategy processes and generally receives materials on our ability to mitigate current and emerging risks, and discusses such matters with our Chief Operating Officer. Our processes require that our audit committee is designated to receive prompt and timely information regarding any cybersecurity incident that meets establishing reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed.

Our cybersecurity risk management and strategy processes, which are discussed in greater detail above, are led by our Chief Operating Officer. This individual has over twenty years of prior work experience in various roles involving managing information security, developing cybersecurity strategy, implementing effective information and cybersecurity programs. The Chief Operating Officer, along with the Company's managed services provider, are informed about and monitor the prevention, mitigation, detection, and remediation of cybersecurity incidents through their management of, and participation in, the cybersecurity risk management and strategy processes described above, including the operation of our incident response plan. As discussed above, the Chief Operating Officer reports to the audit committee of our board of directors about cybersecurity threat risks, among other cybersecurity related matters, at least annually.

Item 2. Properties.

Our corporate headquarters and operations are located in Cambridge, Massachusetts. We currently lease laboratory and office space at 301 Binney Street in Cambridge. 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 12, 2024, there were approximately 68 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 Equity Securities and Use of Proceeds

None.

Issuer Purchases of Equity Securities

There were no repurchases of common stock during the quarter ended December 31, 2023.

Item 6. [Reserved.]

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.

Overview

We are a biopharmaceutical company advancing novel therapeutics to transform the care of serious diseases. We focus on rare metabolic disorders, with our lead program, labafenogene marselecobac (SYNB1934), studied in Synpheny-3, a global, pivotal Phase 3 study for patients with phenylketonuria (PKU), and SYNB1353, a potential treatment for homocystinuria (HCU). Both PKU and HCU are caused by inborn errors of metabolism, and present significant need for innovation due to limitations of both efficacy and safety in the currently available medical treatment options.

In February 2024, we made the decision to discontinue Synpheny-3, our pivotal study of our lead product candidate, labafenogene marselecobac (SYNB1934), as a potential treatment for PKU. The decision to end Synpheny-3 is based on results of an internal review in advance of an upcoming independent Data Monitoring Committee (DMC) assessment, which indicated the trial was unlikely to meet its primary endpoint. The decision was not based on concerns regarding safety or tolerability. We will now work with the Synpheny-3 clinical trial sites involved to implement the discontinuation. As a result, our current corporate strategy is focused on pursuing strategic initiatives to enhance stockholder value, including but not limited to, a merger or the sale of the Company. Our strategic process is both active and ongoing and includes a range of interactions with transaction counterparties. Thus, we believe it is in our stockholders' best interest to allow sufficient opportunity to pursue and consummate one or more such transactions and to consider additional alternatives that may materialize in the future. However, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

Our early-stage pipeline includes product candidates for enteric hyperoxaluria, gout, and cystinuria, and has been fueled by a reproducible, proprietary approach that creates GI-restricted, oral medicines with new enzymatic pathways designed to consume or produce specific biological targets. We design, develop and manufacture these drug candidates, which are produced by applying genetic engineering to well-characterized probiotics.

Our drug candidates are designed through precise engineering to target validated biological pathways in the pathophysiology of a given disease. By using a probiotic to deliver these new enzymatic pathways, the activity is restricted to the gastrointestinal (GI) tract, avoiding systemic exposure and associated risks that limit the success of other modalities. Our pipeline programs are all based on the same probiotic Escherichia coli Nissle 1917, which provides synergies across programs, as well as more than one hundred years of human dosing experience. Our drug candidates are engineered to be non-colonizing, and fully reversible via GI clearance. These potential biopharmaceuticals are all orally administered, conducive to straightforward shipping, distribution and storage. For manufacturing, our platform leverages processes with familiar foundations, including fermentation and lyophilization, facilitating process design and scale-up, combined with unique and proprietary innovations tailored to our unique products.

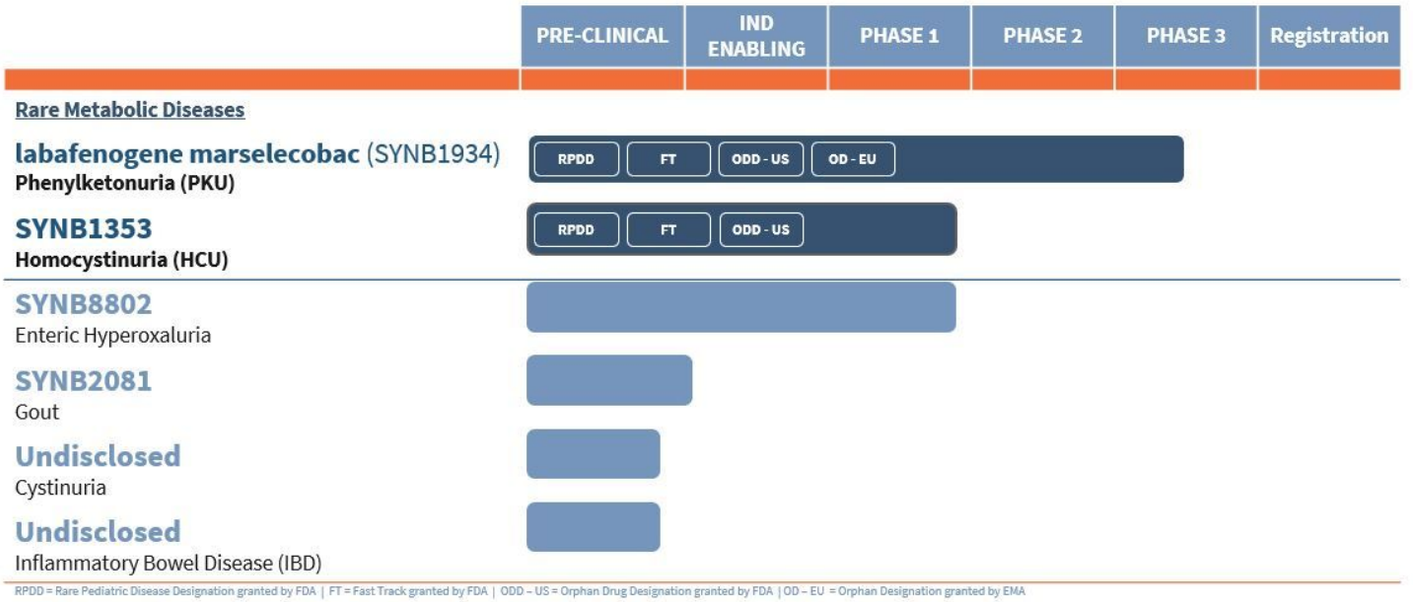
Since our founding, based upon technology from the Massachusetts Institute of Technology (MIT) in 2014, we have progressed a pipeline of multiple drug candidates across different stages, including:

- Labafenogene marselecobac (SYNB1934), which was being studied in Synpheny-3, a pivotal, Phase 3 study for the treatment of patients with PKU;
- SYSYNB1353, a potential treatment for HCU, has achieved proof of mechanism in a Phase 1 study in healthy volunteers;
- Preclinical research activities on a potential drug candidate for cystinuria, a rare, genetic cause of recurrent kidney stones which is also caused by an underlying metabolic disorder;
- SYNB2081, a drug candidate for gout which is in IND-enabling studies; and
- Preclinical research focused on novel, locally-acting, GI-restricted biotherapeutics for indications in inflammatory bowel disease (IBD).

Our Pipeline: Synthetic Biotics in Clinical Development

Our product pipeline consists of drug candidates targeting significant medical needs caused by an underlying metabolic disorder. These include labafenogene marselecobac, which was being evaluated in a pivotal, Phase 3 study in PKU, and drug

candidates designed to treat HCU, enteric hyperoxaluria, and gout. Our preclinical work includes additional metabolic disease research, including cystinuria, target exploration, and focused research efforts in IBD.



Business Overview

We currently operate in one reportable business segment—the discovery and development of Synthetic Biotics. To date, we have dedicated substantially all of our activities to the research and development of our product candidates. We have funded our operations to date primarily with proceeds from the sale of preferred stock, common stock, preferred units, warrants, payments received under the Roche Collaboration and Option agreement, prior collaborations, interest earned on investments, and cash received in the Merger.

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 $57.3 million and $66.1 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023 and 2022, we had an accumulated deficit of approximately $414.3 million and $357.0 million, respectively, and we expect to incur losses for the foreseeable future as we develop our product candidates. Historically, our expenses and capital requirements have increased substantially in connection with our research and development activities, as we:

- Completed preclinical studies, initiated and completed clinical trials for product candidates;
- Contracted to manufacture product candidates;
- Advanced research and development related activities to expand our product pipeline;
- Maintained, expanded and protected our intellectual property portfolio;
- Hired additional staff, including clinical, scientific, commercial and management personnel;
- Expanded our existing infrastructure and secure space in a facility to support continued growth in our research and development efforts; and
- Added 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, finance 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.

Effects of Inflation

We do not believe that inflation has had a material impact on our business or operating results during the periods presented. However, inflation has had, and may continue to have, an impact on the labor costs we incur to attract and retain qualified personnel, costs to conduct clinical trials and other operational costs. Inflationary costs could adversely affect our business, financial condition and results of operations. In addition, increased inflation has had, and may continue to have, an effect on interest rates. Increased interest rates may adversely affect our borrowing rate and our ability to obtain, or the terms under which we can obtain, any potential additional funding.

Financial Overview

Revenue

Revenue for the year ended December 31, 2023 was generated from the Roche Collaboration and Option Agreement. See Note 10, *Collaboration Agreements: Roche Collaboration* 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.

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;
- Leased manufacturing space; 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.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to decrease in the near future as we have discontinued our Synpheny-3 clinical trial and are evaluating strategic options for the Company.

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,	
	2023	2022
Labafenogene marselecobac (SYNB1934)	$ 13,267	$ 4,380
SYNB1618	639	3,436
SYNB8802	976	4,197
SYNB1353	377	2,259
SYNB1891	(135)	1,223
External pre-development candidate costs and unallocated costs	4,225	7,129
Total external costs	19,349	22,624
Internal costs:		
Employee compensation and benefits (including equity-based compensation expense)	13,200	16,515
Facility and other	11,422	12,905
Total internal costs	24,622	29,420
Total research and development expense	$ 43,971	$ 52,044

General and Administrative Expense

General and administrative expenses consist 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 general and administrative costs include the legal costs of pursuing patent protection of our intellectual property, facility and information technology infrastructure costs, directors' and officers' insurance, and professional fees for accounting, tax, legal and consulting services. We anticipate that our general and administrative expenses may increase in the future as we explore strategic alternatives, including potential legal, accounting and advisory expenses and other related charges. We also anticipate that we will continue to incur accounting, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

Other Income (Expense)

Interest and investment income consists of income earned on investments. Interest expense consists of expense related to our finance leases. Other expense consists primarily of gains and losses on foreign currency invoices and losses on remeasurement of the purchase warrant liability.

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

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 to not be at a 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, adjust 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. The estimates we use to record revenue relating to the combined performance obligation on an over time basis, include input methods such as full-time equivalent time incurred compared to the full-time equivalent time expected to be incurred in the future to satisfy the performance obligation, which require management judgment. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. With this method, we must estimate total inputs required to satisfy a performance obligation and measure efforts expended to date to determine revenue recognition. This estimate of remaining inputs is subjective, as the research is novel, and therefore efforts to be successful may be different than the estimated efforts at the balance sheet date.

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 estimate 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 recognize 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 and services are performed.

Warrants

Warrants are accounted for as either derivative liabilities or as equity instruments depending on the specific terms of the agreement. Warrants that are equity-classified instruments and recorded in additional paid-in capital at issuance are not subject to remeasurement. The purchase warrants issued in October 2023 are liability classified and recorded at fair value using the Black-Scholes option-pricing model at issuance, with any subsequent changes in fair value recognized in the consolidated statements of operations. We periodically evaluate changes in facts and circumstances that could impact the classification of warrants.

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,	
	2023	2022
	(in thousands)	
Revenue	$ 3,371	$ 1,180
Operating expenses:		
Research and development	43,971	52,044
General and administrative	14,561	16,555
Total operating expenses	58,532	68,599
Loss from operations	(55,161)	(67,419)
Other income (expense):		
Interest and investment income	2,469	1,267
Interest expense	(1)	(2)
Loss on purchase warrant liability	(4,058)	—
Other expense	(517)	7
Other income (expense), net	(2,107)	1,272
Loss before income taxes	(57,268)	(66,147)
Income tax expense	(14)	—
Net loss	$ (57,282)	$ (66,147)

Year Ended December 31, 2023 Compared to Year Ended December 31, 2022

Revenue

	Years Ended December 31,		Change	
	2023	2022	$	%
	(in thousands)			
Revenue	$ 3,371	$ 1,180	$ 2,191	186%

Revenue was $3.4 million for the year ended December 31, 2023 compared to $1.2 million for the year ended December 31, 2022. Revenue for both periods was primarily related to services performed under the Roche collaboration that we entered into in June 2021.

Operating Expenses

	Years Ended December 31,		Change	
	2023	2022	$	%
	(in thousands)			
Operating expenses:				
Research and development	$ 43,971	$ 52,044	$ (8,073)	-16%
General and administrative	14,561	16,555	(1,994)	(12)%
Total operating expenses	$ 58,532	$ 68,599	$ (10,067)	-15%

Research and Development Expense

Research and development expense was $44.0 million for the year ended December 31, 2023 compared to $52.0 million for the year ended December 31, 2022. The decrease of $8.0 million was due to decreases of clinical development costs of $3.2 million for SYNB8802, $2.8 million for SYNB1618, $1.9 million for SYNB1353, and $1.3 million for SYNB1891. There were additional decreases of $4.8 million in compensation, benefits and other employee-related expenses, $2.9 million in other early development candidates and unallocated costs. These decreases were offset by increases of clinical development costs of $8.9 million for Labafenogene marselecobac (SYNB1934).

General and Administrative Expense

General and administrative expense was $14.6 million for the year ended December 31, 2023 compared to $16.6 million for the year ended December 31, 2022. The decrease of $2.0 million was primarily attributable to decreased professional services costs, and lower compensation, benefits and other employee-related expenses due to reduced headcount.

Other Income (Expense)

	Years Ended December 31,		Change	
	2023	2022	$	%
	(in thousands)			
Other income (expense):				
Interest and investment income	$ 2,469	$ 1,267	$ 1,202	95%
Interest expense	(1)	(2)	1	(50)%
Loss on purchase warrant liability	(4,058)	—	(4,058)	100%
Other expense	(517)	7	(524)	(7486)%
Total other income (expense), net	$ (2,107)	$ 1,272	$ (3,379)	(266)%

Other expense for the year ended December 31, 2023 was $2.11 million compared to other income of $1.30 million for the corresponding period in 2022. The decrease in other income (expense) of $3.4 million was due to an increase in other expense primarily relating to the change in fair value of the purchase warrants classified as liabilities on the consolidated balance sheet. This increase of expense was offset by an increase to income earned on our cash, cash equivalents and short-term investment balances, primarily related to higher interest rates.

Liquidity and Capital Resources

We have incurred losses since our inception on March 14, 2014 and as of December 31, 2023, we had an accumulated deficit of $414.3 million. We have financed our operations to date primarily through the sale of preferred stock, common stock, preferred units and warrants, payments received under collaboration agreements, including the technology collaboration with Ginkgo, the Roche Collaboration and Option agreement, and prior collaborations, interest earned on investments, and cash received in the Merger. At December 31, 2023, we had $47.7 million in cash, cash equivalents, and short-term marketable securities. Our cash and cash equivalents include amounts held in money market funds, stated at cost plus unrealized gain and loss, which approximates fair market value. Our available-for-sale securities include amounts held in commercial paper and U.S. treasuries. 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, 2023, our cash, cash equivalents and marketable securities balance decreased $29.9 million. This decrease was primarily due to 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. These decreases were offset by the proceeds from maturity of marketable securities.

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

	Years ended December 31,	
	2023	2022
	(in thousands)	
Net cash, cash equivalents and restricted cash (used in) provided by		
Operating activities	$ (51,614)	$ (56,888)
Investing activities	38,769	58,351
Financing activities	20,944	(2,040)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 8,099	$ (577)

Cash Flows from Operating Activities

Net cash, cash equivalents and restricted cash used in operating activities was $51.6 million for the year ended December 31, 2023. The primary use of cash was our net loss of $57.3 million and changes in our assets and liabilities of $6.2 million, partially offset by $11.9 million of non-cash items primarily including the change in fair value of purchase warrants, depreciation, equity-based compensation, and the right of use asset. The changes in our assets and liabilities include decreases in the operating lease liability, increases in prepaid expenses and other current assets, decreases in prepaid research and development expenses, decreases in accounts payable and accrued expenses, and decreased deferred revenue.

Net cash, cash equivalents and restricted cash used in operating activities was $56.9 million for the year ended December 31, 2022. The primary use of cash was our net loss of $66.1 million, partially offset by changes in our assets and liabilities of $0.7 million and $8.5 million of non-cash items primarily including depreciation, equity-based compensation, and the right of use asset. The changes in our assets and liabilities include decreases in the operating lease liability, decreases in prepaid expenses and other current assets, increases in prepaid research and development expenses, increases in accounts payable and accrued expenses, and increased deferred revenue.

Cash Flows from Investing Activities

Net cash provided by investing activities for the year ended December 31, 2023 was $38.8 million and resulted primarily from the proceeds from maturity of marketable securities of $66.9 million. This was offset by the purchases of marketable securities of $27.9 million and property and equipment of $0.2 million.

Net cash provided by investing activities for the year ended December 31, 2022 was $58.4 million and resulted primarily from the proceeds from maturity of marketable securities of $141.9 million. This was offset by the purchases of marketable securities of $82.8 million and property and equipment of $0.7 million.

Cash Flows from Financing Activities

Net cash provided by financing activities for the year ended December 31, 2023 totaled $20.9 million, primarily related to net proceeds of $19.6 million from the issuance of our common stock, pre-funded warrants and purchase warrants in an underwritten public offering in October 2023, $1.2 million from the sale of our common stock in the ATM offering program, and $0.1 million of proceeds received from stock option exercises and purchases made pursuant to our employee stock purchase plan.

Net cash used in financing activities for the year ended December 31, 2022 totaled $2.0 million, primarily related to the repurchase of our common stock of $2.5 million, partially offset by $0.3 million from the sale of our common stock in the ATM offering program, and $0.2 million of proceeds received from stock option exercises and purchases made pursuant to our employee stock purchase plan.

Funding Requirements

We currently expect our expenses to decrease in the near term due to our decision to discontinue our Synpheny-3 clinical trial and conduct workforce reductions while we explore strategic alternatives. Pending the outcome of our review of strategic alternatives, should we decide to continue to advance the clinical development of our product candidates, we expect to incur additional costs in connection with such activities.

We have generated revenue from our Roche collaboration and previous collaborations, 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. Absent any other action, we would require additional liquidity to continue operations over the next 12 months, which raises substantial doubt about our ability to continue as a going concern. As discussed in Note 18, Subsequent Events, in February 2024, management and our board of directors approved a plan to discontinue the Synpheny-3 trial, evaluate strategic options and significantly reduce our workforce. We project that this plan will alleviate the substantial doubt that has been raised through significantly decreasing expenses thereby reducing ongoing liquidity needs to enable the continuation of the evaluation of strategic alternatives for at least 12 months from the issuance date of these financial statements.

Our funding requirements will depend on many factors, including, but not limited to, the following:

- the outcome, success, timing and cost of any strategic transactions, business combinations or divestiture;
- 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;
- 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;
- the extent to which our business is adversely impacted by the effects of the coronavirus outbreak or by other health epidemics or pandemics; and
- other risks and uncertainties, including those listed under Part I, Item 1A. “Risk Factors”.

Contractual Commitments and Obligations

We also have certain significant contractual obligations and commitments that require funding. Our commitments for operating leases relate to our lease of office and laboratory space at 301 Binney Street in Cambridge, Massachusetts and the cGMP clean-room space leased from the Azzur Group, LLC, in Waltham, Massachusetts.

In July 2017, we entered into an agreement to lease 41,346 square feet of laboratory and office space at 301 Binney Street in Cambridge, Massachusetts. Annual rent is $3.4 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 $2.9 million. In conjunction with the lease, we established a letter of credit of a $1.0 million.

On December 7, 2018, Synlogic Operating Company, Inc., a wholly-owned subsidiary of the Company, entered into a Statement of Work (the First 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 First SOW, Azzur 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 Initial Term). Azzur also agreed to provide the Company with storage space and personnel support at the Azzur Suite. The total estimated project cost during the Initial Term for access to, and use of, the cleanroom and storage space, and the personnel support and other services, was $4.8 million.

In April 2021, Synlogic entered into a new agreement (the Second SOW) with Azzur which replaced the First SOW. Pursuant to the Second SOW, Synlogic was granted access to, and use of, the Azzur Suite for a period of 20 months, from May 2021 to December 2022 (the Second Term). The Company determined that the agreement contained an embedded lease because the Company controls the use of the Azzur Suite. Accordingly, the fixed and in-substance fixed consideration under the agreement was used to remeasure the right-of-use (ROU) asset and lease liability at the effective date of the Second SOW.

On January 21, 2022, the Company entered into two Statements of Work with Azzur. Pursuant to the first of these SOWs (the Third SOW), the Company has agreed to pay Azzur $0.7 million to renovate and upgrade the cleanroom space at Azzur for the Company's expanded use. The second of these SOWs (the Fourth SOW) replaces the Second SOW that the Company entered into with Azzur on April 29, 2021. The Fourth SOW extends the term of the lease, for the period beginning January 2022 through March 2023 (the Third Term). The Third and Fourth SOWs resulted in an adjustment to the operating lease right-of-use asset and corresponding operating lease liabilities of $1.8 million.

In November 2022, the Company entered into a new agreement (the Fifth SOW) with Azzur that extended the term of the lease, for the period beginning April 2023 through December 2023 (the Fourth Term). The Fifth SOW contains two options to extend the lease, the first option goes through June 2024, and the second option goes through December 2024. The Fifth SOW resulted in an adjustment to the operating lease right-of-use asset and corresponding operating lease liabilities of $1.0 million.

In December 2023, the Company signed an addendum to exercise the First and Second Option to extend the lease as part of the Fifth SOW discussed above. Part of the addendum agreed to new payment terms that supersede the terms per the Fifth SOW with Azzur. The total remaining liability associated with the Azzur lease is approximately $2.2 million as of December 31, 2023.

The Company may terminate the Fifth SOW on three months' prior written notice at any time during the Term. In addition, either party may terminate the Master Services Agreement (including the SOWs) due to a breach by the other party and failure to cure. As of December 31, 2023, the Company is reasonably certain not to exercise the termination option through December 2024.

As we are a clinical stage company, 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.

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 alliances. 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.

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 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.

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-26 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. In addition, our principal executive officer and principal financial officer have concluded that the impact of the COVID-19 pandemic did not impact our ability to maintain our internal controls over financial reporting and disclosure controls and procedures.

Changes in Internal Control

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 year ended December 31, 2023 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, 2023. 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 (2013). Based on our assessment, management believes that, as of December 31, 2023, 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.

On March 18, 2024, our board of directors appointed Antoine Awad, our Chief Operating Officer, as our Principal Executive Officer (principal executive officer). There were no changes to Mr. Awad's employment or compensation arrangements, and (a) there are no understandings or arrangements between Mr. Awad and any other person pursuant to which he was appointed as our Principal Executive Officer and (b) Mr. Awad has no material interest in any transaction or proposed transaction in which we are or are to be a party. Mr. Awad's qualifications and experience were included in the "Executive Officers" section of our Definitive Proxy Statement as filed with the U.S. Securities and Exchange Commission on May 1, 2023, and the description of such qualifications and experience is hereby incorporated by reference.

Additionally, on March 18, 2024, our board of directors appointed May Beth Dooley, age 43, our Head of Finance, as our principal financial officer and principal accounting officer.

Ms. Dooley has served as our Head of Finance since November 2023 and prior to that as our Controller since June 2018. Prior to joining us, Ms. Dooley worked as a senior manager of financial planning analysis at Idera Pharmaceuticals from July 2014 to May 2018, and prior to that, as an associate with PricewaterhouseCoopers from September 2012 to July 2014. Ms. Dooley received a B.A. from Bates College and an M.B.A. and a master's degree in accounting from Northeastern University.

Ms. Dooley previously entered into an offer letter with us dated April 11, 2018 (the "Offer Letter"). She receives a current base salary of $325,000 and is eligible to receive an annual bonus equal to 30% of her annualized base salary. The foregoing description of the material terms of the Offer Letter is qualified in its entirety by the full text of the Offer Letter, a copy of which is filed as an exhibit to this annual report on Form 10-K.

Ms. Dooley has no family relationships with any of our directors or executive officers, and she has no direct or indirect material interest in any transaction required to be disclosed pursuant to Item 404(a) of Regulation S-K. In addition, there are no arrangements or understandings between Ms. Dooley and any other person pursuant to which she was selected as an officer.

Rule 10b5-1 Trading Plans

During the fiscal quarter ended December 31, 2023, none of our directors or executive officers adopted, modified or terminated any contract, instruction or written plan for the purchase or sale of our securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1 (c) or any "non-Rule 10b5-1 trading arrangement."

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections.

Not Applicable.

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 2024 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 2024 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 2024 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 2024 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 2024 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)	05/16/2017	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)	08/28/2017	001-37566
3.3	Certificate of Amendment (Name Change) to the Amended and Restated Certificate of Incorporation		8-K (Exhibit 3.2)	08/28/2017	001-37566
3.4	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Synlogic, Inc., dated June 15, 2023		8-K (Exhibit 3.1)	6/15/2023	001-37566
3.5	Certificate of Amendment (Reverse Stock Split) to the Amended and Restated Certificate of Incorporation of Synlogic, Inc., dated September 27, 2023		8-K (Exhibit 3.1)	9/28/2023	001-37566
3.6	Amended and Restated Bylaws		8-K (Exhibit 3.2)	10/6/2015	001-37566
3.7	Certificate of Designation of Series A Junior Participating Preferred Stock of Synlogic, Inc., as filed with the Secretary of State of the State of Delaware on February 20, 2024.		8-K (Exhibit 3.1)	2/20/2024	001-37566
4.1	Form of Common Stock Certificate		S-1/A (Exhibit 4.2)	09/18/2015	333-206544
4.2	Pre-Funded Warrant		8-K (Exhibit 4.1)	06/12/2019	001-37566
4.3	Form of Pre-Funded Warrant		8-K (Exhibit 4.1)	9/29/2023	001-37566
4.4	Form of Purchase Warrant		8-K (Exhibit 4.2)	9/29/2023	001-37566
4.5	Description of Securities		10-K (Exhibit 4.3)	03/12/2020	001-37566

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
4.6	Rights Agreement, dated as of February 20, 2024, between Synlogic, Inc. and Equiniti Trust Company LLC, as rights agent.		8-K (Exhibit 4.1)	2/20/2024	001-37566
10.1#	2015 Equity Incentive Award Plan		10-K (Exhibit 10.1)	03/20/2018	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))	09/11/2015	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))	09/11/2015	333-206544
10.4#	2017 Stock Incentive Plan		10-K (Exhibit 10.4)	03/20/2018	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	001-37566
10.6#	2023 Inducement Equity Incentive Award Plan	X			
10.7#	Form of Stock Option Grant Notice and Stock Option Agreement under 2023 Inducement Equity Incentive Award Plan	X			
10.8#	Non-Employee Director Compensation Program.		8-K (Exhibit 10.1)	01/31/2020	001-37566
10.9#	Form of Indemnification Agreement between the Company and each of its directors and officers		S-1/A (Exhibit 10.13)	09/11/2015	333-206544
10.10#	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)	08/28/2017	001-37566
10.11#	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)	08/28/2017	001-37566
10.12#	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)	08/28/2017	001-37566
10.13#	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)	08/9/2018	001-37566
10.14#	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
10.15#	Amendment to Employment Agreement dated December 26, 2023, by and between the Company, and Aoife Brennan		8-K (Exhibit 10.1)	12/29/2023	001-37566

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.16#	Separation Agreement by and between Synlogic, Inc. and Aoife M. Brennan, MB, BCh, BAO, MMSc, dated as of February 17, 2024	X			
10.17#	Employment Agreement dated as of January 24, 2022, by and between Synlogic and Michael Jensen		8-K (Exhibit 10.1)	03/03/2022	001-37566
10.18#	Separation Agreement by and between Synlogic, Inc. and Michael Jensen, dated as of November 13, 2023	X			
10.19#	Employment Letter Agreement dated November 28, 2018, by and between Synlogic and Antoine Awad		10-K (Exhibit 10.14.1)	03/25/2021	001-37566
10.20#	Promotion Letter, dated July 21, 2020, for Antoine Awad		10-K (Exhibit 10.14.2)	03/25/2021	001-37566
10.21#	Amendment to Employment Agreement dated December 16, 2023, by and between the Company and Antoine Awad		8-K (Exhibit 10.2)	12/29/2023	001-37566
10.22#	Separation Agreement by and between Synlogic, Inc. and Antoine Awad, dated as of February 17, 2024	X			
10.23#	Retention Bonus Agreement by and between Synlogic, Inc. and Antoine Awad, dated as of March 7, 2024	X			
10.24#	Employment Letter Agreement dated April 11, 2018 by and between Synlogic, Inc. and Mary Beth Dooley	X			
10.25#	Retention Bonus Agreement by and between Synlogic, Inc. and Mary Beth Dooley, dated as of March 7, 2024	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)	08/28/2017	001-37566
10.27	Sales Agreement, dated as of July 23, 2021 by and between the registrant and Jefferies LLC		10-Q (Exhibit 1.1)	11/10/2021	001-37566
10.28†	Master Contract Services Agreement, dated as of September 8, 2018, between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC).		10-K (Exhibit 10.29)	03/12/2019	001-37566
10.29†	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).		10-K (Exhibit 10.30)	03/12/2019	001-37566
10.30†	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).		10-K (Exhibit 10.31)	03/12/2019	001-37566

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.31	Subscription Agreement dated June 11, 2019 by and between the Company and Ginkgo Bioworks, Inc.		8-K (Exhibit 10.1)	06/12/2019	001-37566
10.32†	Foundry Terms of Service Agreement dated June 11, 2019 by and between Synlogic Operating Company Inc. and Ginkgo Bioworks, Inc.		10-Q (Exhibit 10.2)	08/08/2019	001-37566
10.33#	Synlogic, Inc. 2015 Employee Stock Purchase Plan, as amended		8-K (Exhibit 10.1)	12/20/2019	001-37566
10.34†	License and Services Agreement and Statement of Work, dated April 28, 2021, by and between Synlogic Operating Company, Inc. and Azzur Cleanrooms-On-Demand – Boston, LLC.		10-Q (Exhibit 10.1)	08/12/2021	001-37566
10.35†	Pilot Collaboration and Option Agreement, dated June 16, 2021, among Synlogic Operating Company, Inc. and Hoffman-La Roche Inc.		10-Q (Exhibit 10.2)	08/12/2021	001-37566
10.36	Amendment to Pilot Collaboration and Option Agreement, dated as of August 16, 2023, among Synlogic Operating Company, Inc. and Hoffman-La Roche Inc.		10-Q (Exhibit 10.1)	11/09/2023	001-37566
10.37†	Statement of Work dated January 21, 2022 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC), SOW P-10558-01		10-K (Exhibit 10.30)	03/17/2022	001-37566
10.38†	Statement of Work dated January 21, 2022 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC), SOW P-10558-2		10-K (Exhibit 10.31)	03/17/2022	001-37566
10.39†	Statement of Work dated November 22, 2022 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC), SOW P-10558-01 Extension A		10-K (Exhibit 10.32)	03/29/2023	001-37566
10.40†	Addendum to Statement of Work dated December 8, 2023 pursuant to Master Contract Services Agreement between Synlogic, Inc. and Azzur Group (d/b/a Azzur of New England LLC), SOW P-10558-01 Addendum	X			
21.1	Subsidiaries of the registrant	X			
23.1	Consent of Independent Registered Public 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			

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
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	Inline XBRL Instance Document - – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.	X			
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents	X			
104	Cover Page Interactive Data File (embedded within the Inline XBRL 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.
† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the Securities and Exchange Commission.

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 19, 2024

By: /s/ ANTOINE AWAD
Antoine Awad
Principal Executive 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 Antoine Awad and Mary Beth Dooley his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her 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/ ANTOINE AWAD **Antoine Awad**	Principal Executive Officer *(principal executive officer)*	March 19, 2024
/s/ MARY BETH DOOLEY **Mary Beth Dooley**	Head of Finance *(principal financial officer and principal accounting officer)*	March 19, 2024
/s/ PETER BARRETT **Peter Barrett**	Chairman of the Board	March 19, 2024
/s/ MICHAEL BURGESS **Michael Burgess**	Director	March 19, 2024
/s/ MICHAEL HEFFERNAN **Michael Heffernan**	Director	March 19, 2024
/s/ PATRICIA HURTER **Patricia Hurter**	Director	March 19, 2024
/s/ LISA KELLY-CROSWELL **Lisa Kelly-Croswell**	Director	March 19, 2024
/s/ NICK LESCHLY **Nick Leschly**	Director	March 19, 2024
/s/ EDWARD MATHERS **Edward Mathers**	Director	March 19, 2024
/s/ RICHARD P. SHEA **Richard P. Shea**	Director	March 19, 2024

Index to Consolidated Financial Statements of Synlogic, Inc.

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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, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, 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, 2023 and 2022, 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accounting for warrants issued in underwritten public offering

As discussed in Note 8 to the consolidated financial statements, in October 2023 the Company issued and sold, an underwritten public offering, common stock, pre-funded warrants, and common stock warrants to purchase its common stock (purchase warrants). The pre-funded warrants met the criteria for equity classification. The purchase warrants met the definition of a derivative instrument. Upon issuance, the purchase warrants were recorded as a liability at fair value in the amount of $7.1 million.

We identified the evaluation of the Company's accounting for the purchase warrants and pre-funded warrants, specifically the classification as liabilities or equity, as a critical audit matter. A high degree of challenging and complex auditor judgment was required in evaluating the classification of the purchase warrants and pre-funded warrants due to interpretation of complex provisions included within the respective warrant agreements in order to apply the appropriate accounting guidance. Additionally, evaluating the Company's accounting for the purchase warrants and pre-funded warrants required specialized skills and knowledge.

The following are the primary procedures we performed to address this critical audit matter. We obtained and inspected the purchase warrants and pre-funded warrants agreements to identify key terms and conditions within the agreements that were relevant to the classification determination. We involved professionals with specialized skills and knowledge who assisted in:

- assessing whether the Company's technical accounting analyses considered all key terms and conditions of the agreements that were relevant to the classification determination
- evaluating the Company’s interpretation and application of the relevant accounting literature, including consideration of whether certain actions were within the Company’s control, to support the liability classification of the purchase warrants and the equity classification of the pre-funded warrants on the consolidated balance sheet.

/s/ KPMG LLP

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

Boston, Massachusetts
March 19, 2024

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Balance Sheets

(In thousands, except share and per share data)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 23,960	$ 15,861
Short-term marketable securities	23,786	61,768
Prepaid expenses and other current assets	2,161	2,153
Total current assets	49,907	79,782
Property and equipment, net	5,603	7,323
Right of use asset - operating lease	12,102	14,356
Restricted cash	1,097	1,097
Prepaid research and development, net of current portion	6,825	8,300
Other assets	16	7
Total assets	$ 75,550	$ 110,865
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,457	$ 1,785
Accrued expenses	3,000	5,290
Deferred revenue	—	882
Lease liability - operating lease	4,780	4,152
Finance lease obligations	4	13
Purchase warrant liability	11,163	—
Total current liabilities	20,404	12,122
Long-term liabilities:		
Lease liability - operating lease, net of current portion	12,491	16,129
Finance lease obligations, net of current portion	—	4
Total long-term liabilities	12,491	16,133
Commitments and contingencies (Note 14)		
Stockholders' equity		
Common stock, $0.001 par value		
250,000,000 shares authorized as of December 31, 2023 and December 31, 2022; 9,465,949 shares issued and 9,186,157 shares outstanding as of December 31, 2023 and 4,728,874 shares issued and 4,449,082 outstanding as of December 31, 2022	10	5
Additional paid-in capital	459,458	442,303
Accumulated other comprehensive income (loss)	6	(161)
Accumulated deficit	(414,301)	(357,019)
Treasury stock, at cost (279,792 shares at December 31, 2023 and at December 31, 2022)	(2,518)	(2,518)
Total stockholders' equity	42,655	82,610
Total liabilities and stockholders' equity	$ 75,550	$ 110,865

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,	
	2023	2022
Revenue	$ 3,371	$ 1,180
Operating expenses:		
Research and development	43,971	52,044
General and administrative	14,561	16,555
Total operating expenses	58,532	68,599
Loss from operations	(55,161)	(67,419)
Other income (expense):		
Interest and investment income	2,469	1,267
Interest expense	(1)	(2)
Loss on purchase warrant liability	(4,058)	—
Other expense	(517)	7
Other income (expense), net	(2,107)	1,272
Loss before income taxes	(57,268)	(66,147)
Income tax expense	(14)	—
Net loss	$ (57,282)	$ (66,147)
Net loss per share - basic and diluted	$ (8.81)	$ (13.83)
Weighted-average common stock outstanding - basic and diluted	6,502,279	4,781,696
Comprehensive loss:		
Net loss	$ (57,282)	$ (66,147)
Net unrealized gain (loss) on marketable securities	167	(116)
Comprehensive loss	$ (57,115)	$ (66,263)

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Common stock $0.001 par value		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Treasury Stock		Total equity
	Shares	Amount				Shares	Amount	
Balance at December 31, 2021	4,646,590	$ 5	$ 438,178	$ (45)	$ (290,872)	—	$ —	$ 147,266
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	32,097	—	288	—	—	—	—	288
Repurchase of common stock	—	—	—	—	—	(279,792)	(2,518)	(2,518)
Exercise of options	2,370	—	61	—	—	—	—	61
Issuance of restricted stock	50,851	—	—	—	—	—	—	—
Issuance of common stock under employee stock purchase plan	7,108	—	137	—	—	—	—	137
Cancellation of restricted stock	(10,142)	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	3,639	—	—	—	—	3,639
Unrealized gain (loss) on securities	—	—	—	(116)	—	—	—	(116)
Net loss	—	—	—	—	(66,147)	—	—	(66,147)
Balance at December 31, 2022	4,728,874	$ 5	$ 442,303	$ (161)	$ (357,019)	(279,792)	$ (2,518)	$ 82,610
Proceeds from issuance of common stock and accompanying pre-funded warrants, net of issuance costs	3,921,928	$ 4	$ 12,976					$ 12,980
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	115,966		1,249	—	—	—	—	1,249
Exercise of pre-funded warrants	669,126	1	—					1
Issuance of restricted stock	10,803	—	—	—	—	—	—	—
Issuance of common stock under employee stock purchase plan	34,478	—	124	—	—	—	—	124
Cancellation of restricted stock	(15,119)	—	—	—	—	—	—	—
Reverse split: fractional share adjustment	(107)							—
Equity-based compensation expense	—	—	2,806	—	—	—	—	2,806
Unrealized gain (loss) on securities	—	—	—	167	—	—	—	167
Net loss	—	—	—	—	(57,282)	—	—	(57,282)
Balance at December 31, 2023	9,465,949	10	459,458	6	(414,301)	(279,792)	(2,518)	42,655

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31, 2023	Year Ended December 31, 2022
Cash flows from operating activities:		
Net loss	$ (57,282)	(66,147)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,958	2,520
Gain on disposal of property and equipment	(11)	—
Equity-based compensation expense	2,806	3,639
Change in fair value warrant liability	4,058	—
Transaction costs allocated to warrant liabilities	508	—
Accretion/amortization of investment securities	(818)	(772)
Reduction in carrying amount of operating lease right of use asset	3,337	3,149
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(8)	2,568
Prepaid research and development, net of current portion	1,475	1,009
Other assets	(9)	(4)
Accounts payable and accrued expenses	(2,653)	697
Deferred revenue	(882)	351
Operating lease liabilities	(4,093)	(3,898)
Net cash used in operating activities	(51,614)	(56,888)
Cash flows from investing activities:		
Purchases of marketable securities	(27,931)	(82,787)
Proceeds from maturity of marketable securities	66,898	141,866
Purchases of property and equipment	(214)	(728)
Proceeds from the sale of property and equipment	16	—
Net cash provided by investing activities	38,769	58,351
Cash flows from financing activities:		
Payments on finance lease obligations	(13)	(13)
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	1,249	293
Proceeds from employee stock purchases and exercise of stock options	124	198
Proceeds from issuance of common stock, pre-funded warrants and purchase warrants, net of issuance costs	19,583	—
Proceeds from exercise of pre-funded warrants	1	—
Repurchase of common stock (treasury stock)	—	(2,518)
Net cash provided by (used in) financing activities	20,944	(2,040)
Net increase (decrease) in cash, cash equivalents and restricted cash	8,099	(577)
Cash, cash equivalents and restricted cash at beginning of period	16,958	17,535
Cash, cash equivalents and restricted cash at end of period	$ 25,057	$ 16,958
Supplemental disclosure of non-cash investing activities:		
Property and equipment purchases included in accounts payable and accrued expenses	$ 29	$ 27
Assets acquired under operating lease obligation	$ 1,083	$ 3,616
Supplemental disclosure of non-cash financing activities:		
Cash paid for income taxes	$ 14	$ —
Issuance costs included in accounts payable and accrued expenses	$ 6	$ 6
Cash paid for interest	$ 1	$ 2

See accompanying notes to the consolidated financial statements.

SYNLOGIC, INC. AND SUBSIDIARIES

Notes to 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 applying synthetic biology to the discovery and development of Synthetic Biotics. Synthetic Biotics are generated from Synlogic's proprietary platform, leveraging a reproducible, modular approach to the generation of novel drug candidates that perform or deliver critical therapeutic functions. Synthetic Biotics are designed to metabolize a toxic substance, compensate for missing or damaged metabolic pathways or deliver combinations of therapeutic factors. Synlogic's goal is to discover, develop and ultimately commercialize Synthetic Biotics. Since incorporation, the Company has devoted substantially all of its efforts to the research and development of its product candidates.

Going Concern and Liquidity

The Company's consolidated financial statements have been prepared assuming it will continue as a going concern. The going concern assumption contemplates the continuity of operations, and the realization of assets and the satisfaction of liabilities in the ordinary course of business. The Company has historically generated negative cash flows from operations and has an accumulated deficit of $414.3 million at December 31, 2023. At December 31, 2023, the Company had $47.7 million in cash, cash equivalents and short-term marketable securities. Absent any other action, the Company would require additional liquidity to continue its operations over the next 12 months, which raises substantial doubt about the Company's ability to continue as a going concern.

As discussed in Note 18, Subsequent Events, in February 2024, the Company and its board of directors approved a plan to discontinue the Synpheny-3 trial, significantly reduce its workforce and evaluate strategic options for the Company. The Company projects that this plan will alleviate the substantial doubt that has been raised through significantly decreasing expenses thereby reducing ongoing liquidity needs to enable the continuation of the evaluation of strategic alternatives for at least 12 months from the issuance date of these financial statements.

Risks and Uncertainties

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 alliances.

COVID-19

While the Company is not aware of a material impact from the continuation of the COVID-19 pandemic through December 31, 2023, the full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations, and financial condition, including expenses and manufacturing, clinical trials, and research and development costs, depends on future developments that are uncertain at this time.

(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).

Reverse Stock Split

On September 27, 2023, the Company effected a one-for-fifteen reverse stock split of its issued and outstanding common stock, which also adjusted all outstanding warrants. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this stock split. All fractional shares resulting from the reverse stock split were paid in cash.

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 research and development accruals and prepaids, accrued expenses, contingencies, and investments. 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 consist of money market funds, including money market funds held in a sweep account. 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 $24.0 million and $15.9 million at December 31, 2023 and 2022, 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 $1.1 million at December 31, 2023 and 2022 in a letter of credit to secure its lease at the 301 Binney Street facility. The Company has classified this deposit 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, 2023	December 31, 2022
Cash and cash equivalents	$ 23,960	$ 15,861
Restricted cash	1,097	1,097
Total cash, cash equivalents, and restricted cash shown in the consolidated statement of cash flows	$ 25,057	$ 16,958

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, 2023 and 2022.

Available-for-Sale Securities

The Company classifies all of its investments as available-for-sale based upon its intent with regard to such investments. The Company classifies investments as short-term when their remaining contractual maturities are one year or less from the balance sheet date, and as long-term when the investment has a remaining contractual maturity of more than one year from the balance sheet date. 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.

Leases

The Company uses judgement to assess if an arrangement is a lease at contract inception. An arrangement is a lease if the contract involves the use of a distinct identified asset, the lessor does not have substantive substitution rights and the Company obtains control of the asset throughout the period by obtaining substantially all of the economic benefit of the asset and the right to direct the use of the asset. Leases classified as operating leases are included in operating lease right-of-use (ROU) assets, current operating lease liabilities and noncurrent operating lease liabilities in our consolidated balance sheet. Finance leases are included in property and equipment and finance lease obligations in our consolidated balance sheet.

ROU assets represent the right-to-use an underlying asset for the lease term and lease liabilities represent the obligation to make lease payments arising from the lease. ROU assets and lease liabilities are recognized at the lease commencement date based on the estimated present value of lease payments over the lease term. The Company utilizes its incremental borrowing rate to determine the present value of lease payments. The incremental borrowing rate is the rate incurred to borrow similar funds, on a collateralized basis, over a comparable term in a similar economic environment.

The Company has elected to account for the lease and non-lease components for leases as a single component for classes of all underlying assets and allocate all of the contract consideration to the lease component only. Lease cost for operating leases is recognized on a straight-line basis over the lease term and is included in operating expenses on the statements of operations and comprehensive loss. Variable lease payments are included in lease operating expenses.

The lease term includes options to extend the lease when it is reasonably certain that option will be exercised. Leases with a term of 12 months or less are not recorded on the Company's consolidated balance sheet.

Research and Development Costs

Costs incurred in research and development 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 the completion status of the research and development programs and the associated estimate of unbilled costs.

Warrants

The Company accounts for issued warrants either as a liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("ASC 480-10") or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* ("ASC 815-40"). The assessment considers whether the warrants are freestanding financial instruments pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants meet all of the requirements for equity classification under ASC 815, including whether the warrants are indexed to the company's own stock and whether the warrant holders could potentially require "net cash settlement" in a circumstance outside of the company's control, among other conditions for equity classification. This assessment, which requires the use of professional judgment, is conducted at the time of warrant issuance and as of each subsequent quarterly period end date while the warrants are outstanding.

Warrants that are equity-classified instruments and recorded in additional paid-in capital at issuance are not subject to remeasurement. The purchase warrants issued in October 2023 are liability classified and recorded at fair value using the Black-Scholes option-pricing model at issuance, with any subsequent changes in fair value recognized in the consolidated statements of operations. The Company periodically evaluates changes in facts and circumstances that could impact the classification of warrants.

Revenue recognition

The Company was generating revenue through a collaboration and option agreement with Roche for the development and commercialization of product candidates. The Roche Collaboration and Option Agreement concluded after the last milestone was achieved by the Company in October 2023. Subsequently, Roche did not exercise its exclusive option to enter into a licensing and collaboration agreement for further development and commercialization of the product candidate.

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, 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, adjust 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. The estimates we use to record revenue relating to the combined performance obligation on an over time basis, include input methods such as full-time equivalent time incurred compared to the full-time equivalent time expected to be incurred in the future to satisfy the performance obligation, which require management judgment. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. With this method, we must estimate total inputs required to satisfy a performance obligation and measure efforts expended to date to determine revenue recognition. This estimate of remaining inputs is subjective, as the research is novel, and therefore efforts to be successful may be different than the estimated efforts at the balance sheet date.

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, non-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. The fair value of each option and purchase rights under the employee stock purchase plan (ESPP) is estimated on the date of grant using the Black-Scholes option-pricing model. Expected volatility for the Company's common stock is determined based on an average of the historical volatility of the Company and the historical volatility of a peer-group of similar public companies. The expected term of options granted to employees is calculated using the simplified method, which represents the average of the contractual term of the option and the weighted-average vesting period of the option. The expected term of purchase rights for the ESPP is based on the duration of an offering period. 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.

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, outstanding stock options and potential shares issuable under the ESPP.

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.

Treasury Stock

Treasury stock purchases are accounted for under the cost method whereby the entire cost of the acquired stock is recorded as treasury stock.

Recently Issued and Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (FASB) or other accounting standard setting bodies that the Company adopts as of the specified effective date. Unless otherwise discussed below, recently issued pronouncements that are or will be applicable to the Company did not have, or are not expected to have, a material impact on its present or future consolidated financial statements or disclosures.

(3) 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, 2023 and 2022 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, 2023 and 2022, 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, 2023	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 15,476	$ 15,476	$ —	$ —
Commercial paper (included in cash and cash equivalents)	8,484	—	8,484	—
Commercial paper	14,342	—	14,342	—
U.S. government agency securities and treasuries	9,444	6,956	2,488	—
Total	$ 47,746	$ 22,432	$ 25,314	$ —

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 15,861	$ 15,861	$ —	$ —
Commercial paper	44,375	—	44,375	—
U.S. treasuries	17,393	17,393	—	—
Total	$ 77,629	$ 33,254	$ 44,375	$ —

Cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses at December 31, 2023 and December 31, 2022 are carried at amounts that approximate fair value due to their short-term maturities. Finance lease obligations at December 31, 2023 and December 31, 2022 approximate fair value as they bear interest at a rate approximating a market interest rate.

The following tables summarize the estimated fair value of the assets presented within cash and cash equivalents measured at fair value and the gross unrealized holding gains and losses (in thousands):

December 31, 2023	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Money market funds (included in cash and cash equivalents)	$ 15,476	$ —	$ —	$ 15,476
Commercial paper (included in cash and cash equivalents)	8,482	2	—	8,484
Total	$ 23,958	$ 2	$ —	$ 23,960

December 31, 2022	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Money market funds (included in cash and cash equivalents)	$ 15,861	$ —	$ —	$ 15,861
Total	$ 15,861	$ —	$ —	$ 15,861

(4) Available-for-Sale Securities

The following tables summarize the available-for-sale securities held at December 31, 2023 and 2022 (in thousands):

December 31, 2023	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Commercial paper	$ 14,338	$ 4	$ —	$ 14,342
Corporate debt securities	—	—	—	—
U.S. government agency securities and treasuries	9,444	1	(1)	9,444
Total	$ 23,782	$ 5	$ (1)	$ 23,786

December 31, 2022	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Commercial paper	$ 44,437	$ 8	$ (70)	$ 44,375
Corporate debt securities	—	—	—	—
U.S. government agency securities and treasuries	17,492	—	(99)	17,393
Total	$ 61,929	$ 8	$ (169)	$ 61,768

The contractual maturity of all securities held at December 31, 2023 was six months or less. There were two investments in an unrealized loss position at December 31, 2023. The aggregate fair value of the securities in an unrealized loss position at December 31, 2023 and 2022 was $5.4 million and $36.6 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 maturity or 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, 2023.

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

(5) Prepaid Expenses and Other Current Assets

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

	December 31, 2023	December 31, 2022
Prepaid insurance	$ 691	$ 887
Prepaid research and development	788	320
Other prepaid expenses	536	771
Other current assets	146	175
Total prepaid expenses and other current assets	$ 2,161	$ 2,153

(6) Property and Equipment, net

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

	December 31, 2023	December 31, 2022
Laboratory equipment	$ 8,582	$ 9,313
Computer and office equipment	793	793
Furniture and fixtures	500	500
Leasehold improvements	9,820	9,820
Construction in progress	192	37
	19,887	20,463
Less accumulated depreciation	(14,284)	(13,140)
Property and equipment, net	$ 5,603	$ 7,323

Depreciation expense on property and equipment was $2.0 million and $2.5 million in 2023 and 2022, respectively.

(7) Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2023	December 31, 2022
Payroll related	$ 2,556	$ 3,401
Professional fees	290	152
Research and development	91	1,624
Other	63	113
Total accrued expenses	$ 3,000	$ 5,290

(8) Stockholders' Equity

Reverse Stock Split

On September 27, 2023, the Company effected a reverse stock split of its shares of common stock, pursuant to which every fifteen (15) shares of the its issued and outstanding common stock was automatically converted into one (1) issued and outstanding share of common stock without any change in the par value of $0.001 per share. The reverse stock split was approved by the stockholders on September 21, 2023 at a special meeting of stockholders.

October 2023 Financing

On October 3, 2023, the Company issued and sold, through an underwritten public offering:

- 3,921,928 shares of its common stock at a price of $2.84 per share less underwriting discounts and commissions;
- pre-funded warrants to purchase up to 3,472,435 shares of its common stock at a price of $2.839 immediately following the consummation of the offering, and;
- accompanying common stock warrants to purchase up to 7,394,363 shares of its common stock at a price of $3.408 per share exercisable immediately after issuance and expires five years from the date of issuance.

Each share of its common stock and each pre-funded warrant was sold together with a common warrant to purchase one share of its common stock. A holder of pre-funded warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 4.99% (or, upon election by a holder prior to the issuance of any warrants, 9.99%) of the number of shares of common stock outstanding immediately after giving effect to such exercise. The net proceeds to the Company from the sale of common stock and pre-funded warrants through the offering, after deducting the underwriting discounts and commissions and offering expenses payable by the Company, were approximately $19.6 million.

The common stock and pre-funded warrants met the criteria for equity classification. The purchase warrants met the definition of a derivative instrument. Accordingly, upon issuance, the purchase warrants were recorded as a liability at fair value using the Black-Scholes option-pricing model in the amount of $7.1 million. Any subsequent changes in fair value of the purchase

warrants is recognized in the consolidated statements of operations. The residual proceeds were allocated between the common stock and pre-funded warrants based on their relative fair values at the time of issuance. The amount allocated to the pre-funded warrants was recorded as a component of stockholders' equity within additional paid-in capital.

At December 31, 2023, the fair value of the purchase warrants was $11.2 million. Accordingly, a loss on remeasurement of the purchase warrant liability of $4.1 million was recorded in the fourth quarter of 2023. The assumptions used in the Black-Scholes option-pricing model at issuance and at December 31, 2023 were:

	December 31, 2023	At Issuance
Expected Term	4.75 years	5.0 years
Weighted-average, risk free interest rate	3.9%	4.8%
Expected volatility	94.0%	91.1%
Dividend yield	—	—
Strike price	$ 3.41	$ 3.41

Subsequent to their issuance and through December 31, 2023, 669,126 pre-funded warrants have been exercised. None of the purchase warrants have been exercised since their issuance.

At-the-Market (ATM) Offering Program

In July 2021, the Company entered into a sales agreement with Jefferies, LLC (Jefferies) with respect to an ATM, under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having aggregate sales proceeds of up to $50.0 million. Jefferies is not required to sell any specific amount but acts as the Company's sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. During the year ended December 31, 2023, 115,966 shares of common stock were sold pursuant to the sales agreement with Jefferies, resulting in net proceeds of approximately $1.25 million.

Ginkgo Warrants

In June 2019, the Company issued to Ginkgo Bioworks, Inc. (Ginkgo) 422,718 shares of common stock and accompanying Pre-Funded Warrants (the Pre-Funded Warrants) to purchase up to an aggregate of 169,874 shares of common stock, at a combined purchase price per share and Pre-Funded Warrant of $135. The Pre-Funded Warrants have an exercise price of $135 per share, with $134.85 of such exercise price paid at the closing of the offering. The proceeds, net of issuance costs, were approximately $79.9 million, $57.0 million related to the proceeds from sale of the common stock and $22.9 million related to the proceeds from sale of the Pre-Funded Warrants. The Pre-Funded Warrants may be exercised at any time until all of the Pre-Funded Warrants are exercised in full to the extent that, after giving effect to such issuance after exercise, Ginkgo would not beneficially own in excess of 19.99% of the number of shares of common stock outstanding immediately after giving effect to the issuance. The Pre-Funded Warrants were classified as a component of permanent equity and were recorded at the issuance date using a relative fair value allocation method. The Pre-Funded Warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of common shares upon exercise. In addition, such warrants do not provide any guarantee of value or return. In addition, in connection with the issuance to Ginkgo of common stock and Pre-Funded Warrants, the Company expanded its existing collaboration and entered into an agreement with Ginkgo for the research and development of engineered microbial therapeutic products. None of the Pre-Funded Warrants have been exercised as of December 31, 2023. (See Note 10, *Collaboration Agreements*: *Ginkgo Collaboration*).

The Company has reserved for future issuance the following shares of common stock related to the potential exercise of warrants, exercise of stock options, and the employee stock purchase plan:

	December 31, 2023
Common stock issuable under pre-funded warrants	2,803,309
Common stock issuable under purchase warrants	3,921,928
Common stock issuable under Ginkgo pre-funded warrants	169,874
Options exercisable to purchase common stock	311,199
Employee Stock Purchase Plan	19,751
Total	7,226,061

(9) Equity-based Compensation and Equity Incentive Plans

Equity Plans

The Company currently has four active equity plans.

The 2015 Equity Incentive Award Plan (2015 Plan) functions as the primary equity plan for the Company. 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. On January 1, 2023, the Company added 222,454 shares to the 2015 Plan pursuant to the "evergreen provision". 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 (the 2017 Plan) provides for the grant of incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and other stock-based awards.

The 2015 Employee Stock Purchase Plan (ESPP) 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. In December 2019, the Board reactivated the 2015 ESPP and approved an amendment to the ESPP to (i) reduce the permitted payroll deduction and number of shares of the Company's common stock that a participant may purchase per calendar year and offering period under the ESPP and (ii) establish a period for enrollment for eligible participants. The reactivation of the 2015 ESPP was effective immediately. The Company's executive officers are eligible to participate in the 2015 ESPP. The ESPP includes an "evergreen provision," allowing for an annual increase in the number of shares of common stock available for issuance. On January 1, 2023, the Company added 44,490 shares to the ESPP pursuant to the "evergreen provision". There were 34,478 shares of common stock purchased under the ESPP during the year ended December 31, 2023.

The 2023 Inducement Equity Incentive Award Plan (the 2023 Inducement Plan) was established as of December 8, 2023 to provide for the granting of equity awards to individuals who were not previously employees of Synlogic, or following a bona fide period of non-employment, as an inducement material to such individuals' entering into employment with Synlogic, pursuant to Nasdaq Listing Rule 5635(c)(4). No shares were issued under the 2023 Inducement Plan during the year ended December 31, 2023.

Stock Options

The weighted average assumptions used in the Black-Scholes option-pricing model for stock options issued to employees and non-employees under the 2015 Plan and the 2017 Plan, during the years ended December 31, 2023 and 2022 were:

	Year ended December 31,	
Employees:	**2023**	**2022**
Expected term	6.2 years	6.2 years
Weighted-average, risk-free interest rate	3.7%	2.4%
Expected volatility	82.4%	82.5%
Dividend yield	—	—

The following table summarizes stock option activity 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, 2022	482,166	$ 54.78	8.1	$ 30
Granted	305,010	9.28		—
Exercised	—	—		—
Cancelled/Forfeited	(174,415)	24.94		—
Outstanding at December 31, 2023	612,761	9.13	7.8	$ 1,026
Vested or expected to vest at December 31, 2023	612,761	$ 9.13	7.8	$ 1,026
Exercisable at December 31, 2023	311,199	$ 15.62	6.9	$ 464

[(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, 2023 and 2022. 512,972 and 12,364 options were in the money at December 31, 2023 and 2022, respectively.

The weighted average grant date fair value per share of options granted during the years ended December 31, 2023 and 2022 was approximately $6.07 and $13.06, respectively. The total fair value of awards that vested during the years ended December 31, 2023 and 2022 was $2.5 million and $1.2 million, respectively.

As of December 31, 2023, there was approximately $3.2 million of unrecognized share-based compensation for unvested stock option grants which is expected to be recognized over a weighted average period of 2.25 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur.

On November 9, 2023, the Company's board of directors approved a stock option repricing, which repriced certain outstanding stock options held by then current employees. There were 539,685 outstanding eligible stock options that were amended to reduce such exercise price to $1.85 per share, the current fair market value of the Company's common stock on the date of the approval of the repricing. Except for the modified exercise price, all other terms and conditions of each of the eligible stock options remained in full force and effect. The repricing was recorded as a stock option modification whereby the incremental fair value of each option was determined using the Black-Scholes option-pricing model at the date of the modification, and $0.2 million was recognized related to vested options as incremental equity-based compensation expense during the year ended December 31, 2023. The Company is recognizing the remaining $0.2 million of incremental equity-based compensation expense on a straight-line basis over the remaining requisite service period of the stock options.

Restricted Common Stock

During the years ended December 31, 2023 and 2022, 10,803 and 50,851 shares of restricted common stock were granted, respectively.

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, 2022	55,005	$ 28.42
Granted	10,803	9.30
Vested	(14,643)	30.36
Forfeited	(15,119)	20.46
Unvested at December 31, 2023	36,046	$ 25.24

The total fair value of shares that vested during the years ended December 31, 2023 and 2022 was $0.4 million and $0.2 million, respectively.

As of December 31, 2023, there was approximately $0.6 million of unrecognized share-based compensation related to restricted stock awards granted, which is expected to be recognized over a weighted average period of 2.0 years. The total unrecognized share-based compensation cost will be adjusted for actual forfeitures as they occur.

Employee Stock Purchase Plan

The ESPP is considered a compensatory plan with the related compensation expense recognized over the six-month offering periods. The compensation expense for the years ended December 31, 2023 and December 31, 2022 was less than $0.1 million in both years.

Equity Compensation

The Company has recorded total equity-based compensation expense of approximately $2.8 million and $3.6 million, during the years ended December 31, 2023 and 2022, respectively. Equity compensation during the years ended December 31, 2023 and 2022 is derived from stock options, restricted stock awards, and the ESPP.

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, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Research and development	$ 1,024	$ 1,565
General and administrative	1,782	2,074
	$ 2,806	$ 3,639

The following table summarizes equity-based compensation expense by type of award for the years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Stock options	$ 2,354	$ 3,168
Restricted stock awards	362	396
ESPP	90	75
	$ 2,806	$ 3,639

(10) Collaboration Agreements

Roche Collaboration

In June 2021, the Company entered into a Pilot Collaboration and Option Agreement (the Roche Collaboration and Option Agreement) with F. Hoffmann-La Roche Ltd (Roche Basel) and Hoffmann-La Roche Inc. (Roche US, and together with Roche Basel, Roche). Under the terms of the Roche Collaboration and Option Agreement, the Company and Roche will seek to collaborate to research and pre-clinically develop Synthetic Biotics for addressing an undisclosed novel target for the treatment of inflammatory bowel disease (the Product Candidate).

Pursuant to the Roche Collaboration and Option Agreement, Roche agreed to pay the Company, an upfront, nonrefundable technology access fee of $1.0 million, which the Company received in July 2021. In addition, the Company was eligible to receive up to $5.0 million in milestone payments upon the achievement of certain success criteria. Following the research period, Roche holds an exclusive option right (the Option) to negotiate a definitive Collaboration and License Agreement (CLA) for further development and commercialization of the Product Candidate.

Pursuant to the Roche Collaboration and Option Agreement, during the term of such agreement, each party has granted to the other party a non-exclusive, non-transferrable, non-sublicensable, royalty-free right and license to certain intellectual property and know-how controlled by such party, solely as necessary for the party to perform its obligations under the Roche Collaboration and

Option Agreement. The parties will establish a Joint Research Committee (JRC) to oversee and manage the execution of the underlying study plan for the Roche Collaboration and Option Agreement.

The Roche Collaboration and Option Agreement includes various representations, warranties, covenants, indemnities, and other customary provisions. Roche may terminate the Roche Collaboration and Option Agreement without cause immediately upon written notice where certain success criteria have been met for parts of the study plan, or upon ninety (90) days' prior written notice to the Company. Either party may terminate the Roche Collaboration and Option Agreement in the event of an uncured material breach of the other party.

The research and development was estimated to be performed by the Company for approximately two years according to three phases of research as defined in the research plan. The Company was eligible to receive milestone payments from Roche upon the achievement of success criteria for respective milestones.

The Company assessed this arrangement in accordance with ASC 606, *Revenue from Contracts with Customers,* and concluded that the contract counterparty, Roche, is a customer. The Company identified the following material promises made by the Company to Roche 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; (3) implicit renewal options created by Roche's decision not to terminate the contract; (4) the Company's participation on the JRC; and (5) an exclusive right to negotiate a definitive CLA for further development and commercialization of the Product Candidate. The Company determined that the license and research and development activities were not distinct from one another, as the license has limited value without the performance of research and development activities. The Company's participation on the JRC was determined to be quantitatively and qualitatively immaterial and therefore is excluded from performance obligations. As such, the Company determined that the promises associated with the license and research and development services should be combined into a single performance obligation.

The Company next evaluated the milestone payments relating to the three phases of research as defined in the research plan and the option to negotiate and enter into the CLA, to determine whether they provide Roche with any material rights. The Company concluded that the option was 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 Roche 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 Roche Collaboration and Option Agreement, which consists of: (1) the non-exclusive license and (2) the research and development activities.

At the outset of the arrangement, the transaction price included only the $1.0 million up-front consideration received and which was allocated to the single performance obligation. The milestone payments that may be received are excluded from the transaction price until each respective milestone has been achieved. The Company will reevaluate 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 June 2021, the Company began work on the research and development services for the first phase of the research plan and the $1.0 million upfront payment was recognized over the time of the first phase of the research plan. In September 2021, the Company completed the research and development services for the first phase of the research plan and achieved a milestone payment of $1.0 million, which was paid by Roche in November 2021. At this time, the milestone payment was allocated to a new performance obligation consisting of the underlying research and development services to be performed over the second phase of the research plan. In August 2022, the Company completed the research and development services for the second phase of the research plan and achieved a milestone payment of $1.5 million, which was paid by Roche in October 2022. At this time, the milestone payment was allocated to a new performance obligation consisting of the underlying research and development services to be performed over the third phase of the research plan. Upon the Company's completion of these activities and subject to Roche's termination right, the additional milestone payments based on the achievement of specific events outlined in the Roche Collaboration and Option Agreement will become due.

In October 2023, the Company achieved its third pre-specified research milestone under the terms of the Roche Collaboration and Option Agreement and earned a third milestone payment of $2.5 million, which was paid by Roche in December 2023.

Revenue associated with performance obligations under the Roche Collaboration and Option Agreement are recognized as the research and development services are provided using an input method, according to the full-time equivalents incurred. 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.

The Company recognized $3.4 million and $1.2 million for the years ended December 31, 2023 and 2022, respectively, as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss. There was no deferred revenue from the collaboration as of December 31, 2023. The Roche Collaboration and Option Agreement concluded after the last milestone was achieved by the Company in October 2023. Subsequently, Roche did not exercise its exclusive option to enter into a licensing and collaboration agreement for further development and commercialization of the product candidate.

Ginkgo Collaboration

In 2017, the Company established a technology collaboration with Ginkgo. In June 2019, in connection with the issuance to Ginkgo of an aggregate of 422,718 shares of common stock and Pre-Funded Warrants to purchase an aggregate of 169,874 common stock (See Note 8), the Company expanded its collaboration and entered into an agreement with Ginkgo for the research and development of engineered microbial therapeutic products. Under the 2019 expanded agreement, the Company made a prepayment to Ginkgo of $30.0 million for its foundry services that will be provided to the Company over an initial term of five years. The current and non-current balances relating to the prepayment of foundry services is recorded in prepaid expenses and other current assets and prepaid research and development, net of current portion, respectively, on the December 31, 2023 consolidated balance sheet. At December 31, 2023, the Company had remaining balances of $0.3 million and $4.9 million of current and non-current pre-paid research and development costs related to this transaction, respectively. Upon the expiration of such initial term and, if applicable, an additional period, any portion of the prepayment that has not been used to purchase services from Ginkgo will be retained by Ginkgo.

(11) Net Loss per Share

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

	2023	2022
Numerator:		
Net loss	$ (57,282)	$ (66,147)
Denominator:		
Weighted-average common shares outstanding - basic and diluted	6,502,279	4,781,696
Net loss per share - basic and diluted	$ (8.81)	$ (13.83)

The Company's potentially dilutive shares, which include purchase warrants, outstanding stock options, unvested restricted common stock and potential shares issuable under the ESPP, 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,	
	2023	2022
Purchase warrants	3,921,928	—
Unvested restricted common stock awards	36,046	55,005
Outstanding options to purchase common stock	612,761	482,166
Potential shares issuable under the ESPP	19,751	3,508

(12) Income Taxes

During the years ended December 31, 2023 and 2022, the Company recorded no income tax benefits for the net operating losses incurred due to its uncertainty of reclaiming a benefit for those losses.

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,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 87,396	$ 81,803
Tax credit carryforwards	10,401	9,118
Accrued expenses	84	127
Property and equipment	1,113	888
Lease liabilities	4,718	5,541
Equity compensation	3,270	2,516
Amortizable intangibles	1,100	1,165
Amortizable research expenditures [(1)]	20,202	12,000
Other	77	363
Gross deferred tax assets	128,361	113,521
Deferred tax liabilities:		
Right of use assets	(3,306)	(3,922)
Gross deferred tax liabilities	(3,306)	(3,922)
Valuation allowance	(125,055)	(109,599)
Net deferred tax assets	$ —	$ —

[(1)] *Under the Tax Cuts and Jobs Act (TCJA), research and experimental (R&D) expenditures are capitalized and amortized under section 174 for tax years beginning after December 31, 2021. These costs are amortized for tax purposes over 5 years since the R&D was performed in the U.S. The unamortized balance of these costs is presented as a deferred tax asset in the table above.*

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 $125.1 million and $109.6 million was established at December 31, 2023 and 2022, respectively.

A reconciliation of the statutory federal income tax rate to the Company's effective income tax rate is as follows:

	Years ended December 31,	
	2023	2022
	Tax Rate	Tax Rate
U.S. federal statutory rate	21%	21%
State income taxes, net of federal benefit	6%	6%
Other permanent differences	(2)%	(1)%
Tax credits	2%	3%
Other items	0%	0%
Net change in valuation allowance	(27)%	(29)%
Effective income tax rate	—	—

A roll-forward of the valuation allowance for the years ended December 31, 2023 and 2022 is as follows (in thousands):

	Years ended December 31,	
	2023	2022
Balance at beginning of year	$ (109,599)	$ (90,477)
Increase in valuation allowance	(15,456)	(19,122)
Balance at end of year	$ (125,055)	$ (109,599)

As of December 31, 2023, the Company had federal net operating loss carryforwards that may be available to reduce future taxable income of $323.5 million. Of the $323.5 million of federal net operating loss carryforwards, $79.4 million will expire on various dates from 2034 to 2037. The remaining $244.1 million of federal net operating loss carryforwards do not expire. The Company also had state net operating loss carryforwards that may be available to reduce future taxable income of $308.0 million for the period ended December 31, 2023. The state net operating loss carryforwards begin to expire in 2029. In addition, as of December 31, 2023, the Company had federal and state research and development tax credit carryforwards available to reduce future tax liabilities of $7.1 million and $4.2 million, respectively.

On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 into law which contained provisions that include a 15% corporate minimum tax effective for taxable years beginning after December 31, 2022 and a 1% excise tax on certain stock buybacks after December 31, 2022. The Company expects the impact of these provisions to be immaterial.

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. 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 the 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, 2023. The Company's policy is to record interest and penalties related to unrecognized tax benefits on the income tax expense line in the consolidated statement of operations. There are no interest or penalties accrued at December 31, 2023 and 2022.

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 2020 to the present are open to examination under the statute. The Company's net operating losses and other attributes generated in a closed tax year may still be adjusted to determine the amount of carryforward deduction available in an open year under examination.

(13) Share Repurchase

On November 25, 2022, the Company entered into a definitive share repurchase agreement with a stockholder, as part of a privately negotiated transaction, to repurchase 279,792 shares of common stock held by them for an aggregate purchase price of $2.5 million, or $9.00 per share. This repurchase was completed on November 28, 2022.

Repurchased shares are held as treasury stock at cost until they are retired or re-issued. There were no retirements or re-issuances of treasury stock during the year ended December 31, 2023.

(14) Leases

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 $3.4 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. The Company has paid for tenant improvements of approximately $2.9 million. Additionally, the Company has capitalized approximately $6.6 million of landlord-funded tenant improvements. The Company was deemed to be the accounting owner of the tenant improvements primarily because it was responsible for project cost overruns, and as such, the amounts were recorded as a leasehold improvement. The landlord-funded tenant improvement allowance is being amortized as a reduction to lease expense ratably over the lease term. 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. Variable payments based on our portion of the operating expenses, including real estate taxes and insurance, are recorded as a period expense when incurred. The Company has an option to extend the term by five years and an option to terminate the agreement if a similar agreement is executed with the landlord or an affiliate of the landlord. Neither option is reasonably certain of exercise and both are excluded from the lease liability calculation.

During the year ended December 31, 2018, the Company entered into an agreement (the First SOW) with Azzur Group, LLC (Azzur) whereby Azzur 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 Initial Term). In April 2021, Synlogic entered into a new agreement (the Second SOW) with Azzur which replaced the First SOW. Pursuant to the Second SOW, Synlogic was granted access to, and use of, the Azzur Suite for a period of 20 months, from May 2021 to December 2022 (the Second Term). On January 21, 2022, the Company entered into two agreements with Azzur. Pursuant to the first of the agreements (the Third SOW), the Company has agreed to pay Azzur $0.7 million to renovate and upgrade the cleanroom space at Azzur for the Company's expanded use. The second of the agreements (the Fourth SOW) replaces the Second SOW that the Company entered into with Azzur in April 2021. The Fourth SOW extends the term of the lease, for the period beginning January 2022 through March 2023 (the Third Term). In November 2022, the Company entered into a new agreement (the Fifth SOW) with Azzur that extended the term of the lease, for the period beginning April 2023 through December 2023 (the Fourth Term). The Fifth SOW contains two options to extend the lease, the first option goes through June 2024, and the second option goes through December 2024. The Company determined that the agreement contained an embedded lease because the Company controls the use of the Azzur Suite. Accordingly, the fixed and in-substance fixed consideration under the agreement was used to measure the ROU asset and lease liability at the effective date. In December 2023, the Company signed an addendum to exercise the First and Second Option to extend the lease as part of the Fifth SOW discussed above. Part of the addendum agreed to new payment terms that supersede the terms per the Fifth SOW with Azzur. The ROU asset and lease liability are subsequently remeasured to reflect the impact of each subsequent modification.

Leases classified as operating leases are included in operating lease ROU assets, current operating lease liabilities and noncurrent operating lease liabilities in our consolidated balance sheets. The operating lease right-of-use asset and operating lease liability represents the Binney Street lease and the Azzur Suite lease. Cash paid for amounts included in the present value of operating lease liabilities was $5.6 and $5.5 million during the years ended December 31, 2023 and 2022, respectively, which is included in operating cash flows.

The components of lease cost for operating leases for the years ended December 31, 2023 and 2022 were (in thousands):

	For the year ended December 31,	
Operating leases	**2023**	**2022**
Operating lease cost	$ 4,869	$ 4,812
Variable lease cost	1,583	1,409
Total lease cost	$ 6,452	$ 6,221

The right-of-use asset for the operating lease is disclosed on the consolidated balance sheets.

The weighted average remaining lease term and the weighted average discount rate for operating leases were:

	For the year ended December 31,	
	2023	**2022**
Weighted average discount rate	8.3%	8.3%
Weighted average remaining lease term (years)	4.2	5.1

The following table reconciles the undiscounted cash flows for the operating leases at December 31, 2023 to the operating lease liabilities recorded on the balance sheet: December 31, 2023

Maturity of lease liabilities	Operating Leases (in thousands)
2024	$ 5,977
2025	3,791
2026	3,905
2027	4,022
2028	2,667
Thereafter	—
Total lease payments	20,362
Less: imputed interest	3,091
Total lease liabilities	$ 17,271
Current lease liabilities	4,780
Long-term lease liabilities	12,491

The lease cost for finance leases during the years ended December 31, 2023 and 2022, and the finance lease liability at December 31, 2023, were not material.

(15) Commitments and Contingencies

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.

(16) 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 started to match employee contributions effective January 1, 2019. The Company matched 50% of the employee contributions to the 401(k) plan up to a maximum of 4% of the participating employee's eligible earnings, resulting in a maximum company match of 2% of the participating employee's eligible earnings, and subject to certain additional statutory dollar limitations. In 2021, the Company increased the match to 50% of the employee contributions up to a maximum of 6% of the participating employee's eligible earnings, resulting in a maximum company match of 3% of the participating employee's eligible earnings, and subject to certain additional statutory dollar limitations. For the years ended December 31, 2023 and 2022, the Company made $0.3 million and $0.5 million contributions to the plan, respectively.

(17) Related-Party Transactions

In June 2019, the Company expanded its collaboration and entered into an agreement with Ginkgo for the research and development of engineered microbial therapeutic products. As of December 31, 2023, Ginkgo owns 422,718 shares of the Company's outstanding common stock. See Note 10, Collaboration Agreements: Ginkgo Collaboration.

Under the agreement the Company made a prepayment to Ginkgo of $30.0 million for its foundry services that will be provided to the Company over an initial term of five years. At December 31, 2023, the Company had remaining balances of $0.3 million and $4.9 million of current and non-current pre-paid research and development costs related to this transaction, respectively. For the year ended December 31, 2023, the Company used $3.1 million of the pre-paid research and development expense**s.**

(18) Subsequent Events

In February 2024, the Company and its board of directors decided to discontinue the Synpheny-3 trial and significantly reduce its workforce and as a result have made the decision to evaluate strategic options for the Company with a goal to enhance stockholder value, including the possibility of a merger or sale of the Company. The Company expects to devote significant time and resources to

identifying and evaluating strategic alternatives, however, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value**.**

The Company is currently evaluating the impact that this subsequent event will have on the financial statements for the interim period ending March 31, 2024. However, it expects that material restructuring charges will be recorded in addition to material impairment charges, including (but not limited to) impairment charges relating to the balances of property and equipment, net, prepaid research and development costs and right of use assets – operating lease.