UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

OR

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

For the transition period from _____ to _____

Commission File Number: 001-38550

Translate Bio, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**61-1807780**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
29 Hartwell Avenue Lexington, Massachusetts	**02421**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 945-7361

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

Common Stock, $0.001 par value	**The Nasdaq Global Select Market**
(Title of each class)	**(Name of each exchange on which registered)**

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

None
(Title of class)

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Select Market on June 29, 2018, was $215,756,427.

The number of shares of Registrant's common stock outstanding as of March 14, 2019 was 45,273,722.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to its 2019 Annual Meeting of Stockholders, scheduled to be held on June 18, 2019, are incorporated by reference into Part III of this Report.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue" "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- our ability to continue as a going concern;
- our plans to develop our product candidates;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for our product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and short-term investments and proceeds from this offering;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed or incorporated by reference hereto completely and with the understanding that our actual future results may be materially different from what we

expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date hereof, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

PART I

Item 1. Business.

Overview

We are a clinical-stage messenger RNA, or mRNA, therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction. Using our proprietary mRNA therapeutic platform, or MRT platform, we create mRNA that encodes functional proteins. We believe that the mRNA design, delivery and manufacturing capabilities of our MRT platform provide us with the most advanced platform for developing product candidates that deliver mRNA encoding functional proteins for therapeutic uses. Our mRNA is delivered to the target cell where the cell's own machinery recognizes it and translates it, restoring or augmenting protein function to treat or prevent disease. We believe that our MRT platform is broadly applicable across multiple diseases in which the production of a desirable protein can have a therapeutic effect. We are initially focused on restoring the expression of intracellular and transmembrane proteins, areas that have eluded conventional protein therapeutics, in patients with genetic diseases where there is high unmet medical need.

We are developing our lead MRT product candidate for the lung, MRT5005, for the treatment of cystic fibrosis, or CF. We are conducting a Phase 1/2 clinical trial to evaluate the safety and efficacy of MRT5005 and anticipate reporting interim data from this trial in the second half of 2019. We are developing our lead MRT product candidate for the liver, MRT5201, for the treatment of ornithine transcarbamylase, or OTC, deficiency. In December 2018, we submitted an investigational new drug application, or IND, for MRT5201, which the U.S. Food and Drug Administration, or FDA, has placed on clinical hold. The FDA is requiring additional preclinical toxicology data. We have identified the additional preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019. We believe that our MRT platform is distinct from other mRNA-based technologies and has the potential to provide clinical benefits by transforming life-threatening illnesses into manageable chronic conditions.

mRNA plays a central role in the production of proteins, which are needed to carry out essential cellular functions. mRNA transcribes genetic information encoded in DNA into instructions that are used by cells to produce proteins. mRNA therapy is engineered to deliver mRNA encoding natural, functional proteins that replace defective or missing proteins, and has potential advantages, including that it:

- restores gene expression without entering the cell nucleus or changing the genome;
- enables the treatment of diseases that were previously undruggable by using the cell's own machinery to produce natural and fully functional proteins;
- has drug-like properties that are familiar to health care providers, including the potential to repeat and adjust dosing in a chronic setting; and
- permits rapid development from target gene selection to product candidate.

Our product candidates consist of two major components: the protein-coding mRNA and a delivery vehicle. Once we have established delivery capability to a target tissue, we can design new product candidates that vary only in the mRNA sequence, which we expect will allow for rapid target and development candidate identification. We believe that this will enable our MRT platform to be flexible and scalable as we develop additional product candidates. We engineer our mRNA sequences for enhanced stability and to provide for optimal expression of desired proteins. Our mRNA is manufactured by a proprietary, cell-free, enzyme catalyzed process using structural components that are identical to natural mRNA within the body. We then formulate the product candidate by packaging our biosynthetic mRNA into proprietary lipid-based nanoparticle, or LNP, delivery vehicles that are optimized for distribution to specific tissues. We are initially focused on the development of product candidates to treat diseases of the lung and liver. We also believe that our platform has the potential to apply across a broad array of diseases and target tissues. In our preclinical studies, we have observed targeted delivery to the eye, central nervous system, or CNS, lymphatic system and circulatory system, as well as the ability of our platform to enable the production of antibodies. Additionally, we have observed significant improvements in mRNA potency and delivery when compared to prior generations of our mRNA technology as well as competing approaches.

Our MRT platform has been in development for over 10 years, initially at Shire Human Genetic Therapies, Inc., or Shire, a subsidiary of Shire plc. We acquired the MRT platform from Shire in December 2016 and have dedicated substantial resources to the further development of the platform and product candidates. The scientific founders of the MRT platform who were responsible for the research, development, manufacturing and delivery know-how and intellectual property supporting this platform joined our company as part of the acquisition. We have been building upon Shire's pioneering work and significant investment by advancing our product candidates towards clinical trials. We believe these efforts have positioned us as a leading company in mRNA therapeutic development worldwide.

We are developing our lead MRT product candidate for the lung, MRT5005, for the treatment of patients with CF, which is the most common fatal inherited disease in the United States. CF affects approximately 30,000 patients in the United States and a total of more than 70,000 patients worldwide and leads to premature death. CF is caused by genetic mutations that result in dysfunctional or absent cystic fibrosis transmembrane conductance regulator, or CFTR, protein. CF results in mucus buildup in the lungs, pancreas and other organs, and mortality is primarily driven by a progressive decline in lung function. There remains a large unmet medical need in the CF patient population as currently approved CFTR modulating therapies are limited to patients with specific genetic mutations and patients treated with these therapies still suffer from long-term decline in lung function and exacerbations that require hospitalization.

We believe MRT5005 is the first clinical-stage mRNA product candidate designed to deliver mRNA encoding fully functional CFTR protein to the lung. MRT5005 is being developed to treat all patients with CF, regardless of the underlying genetic mutation. This broad applicability is in contrast to CFTR protein modulators currently marketed or in clinical development, which are only effective in a subset of patients with specific genetic mutations, including those with limited or no CFTR protein.

We have designed MRT5005 to be inhaled via a handheld nebulizer and to be administered in a once-weekly dose. Once the inhaled MRT5005 has entered the epithelial cells lining the patient's lungs, our therapeutic mRNA uses the cells' own machinery for translation and expression of fully functional CFTR protein, thereby restoring this essential ion channel, which we believe will address the pathology of CF directly. In our preclinical studies we have observed dose-dependent increases in CFTR being restored to cell membranes and that the inhaled formulation of MRT5005 resulted in broad CFTR expression in lung tissue. We have initiated a double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005 in which we plan to enroll at least 32 patients with CF. In late May 2018, we began enrolling and dosing patients in the single-ascending dose part of this trial. In January 2019, we announced that we received approval from the Protocol Safety Review Committee to initiate the multiple-ascending dose, or MAD, portion of the trial and in February 2019, we announced that dosing of patients in the MAD portion of the trial had begun. We anticipate reporting interim data from the Phase 1/2 clinical trial in the second half of 2019. In 2015, the FDA granted orphan drug designation to MRT5005 for the treatment of CF.

We are advancing our lead MRT product candidate for the liver, MRT5201, for the treatment of patients with OTC deficiency, a metabolic liver enzyme disorder that results from a mutation in the OTC gene. OTC deficiency is the most common urea cycle disorder. This enzyme is an intracellular protein necessary for preventing the accumulation of ammonia, a normal byproduct of protein breakdown. When the enzyme is defective or absent, high levels of ammonia accumulate in the blood, which can cause serious and irreversible neurological damage. The incidence of OTC deficiency is estimated to be 1 in 56,500 live births in the United States.

We have designed MRT5201 for intravenous delivery of mRNA encoding fully functional OTC enzyme to the liver to enable hepatocytes, the predominant type of liver cell, to produce normal OTC enzyme. We expect that sufficient expression of the functional OTC enzyme in hepatocytes would reduce or eliminate the need for current treatments such as strict low-protein diets or ammonia scavengers. We have conducted preclinical studies in OTC-deficient mice in which we have observed delivery of MRT5201 and expression of functionally active human OTC in the mouse liver. Furthermore, MRT5201 was observed to normalize levels of urinary orotic acid, a biomarker of the disease, in these mice and render them resistant to the introduction of ammonia from outside the body for up to four weeks. In December 2018, we submitted an IND to the FDA to support the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Subsequently, the FDA notified us that our IND for MRT5201 was placed on clinical hold. Prior to initiation of our planned Phase 1/2 clinical trial, the FDA is requiring additional preclinical toxicology data to assess the potential for adverse effects related to the clearance time of MRT5201. We have identified the additional preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019. In 2018, MRT5201 was granted orphan drug designation for the treatment of OTC deficiency in the United States and European Union.

In addition to genetic diseases of the lung and liver, we continue to explore other tissues where we believe we can leverage the broad applicability of our MRT platform across multiple diseases in which the production of desirable protein can have a therapeutic effect.

Beyond our two lead product candidates, we continue to advance our discovery-stage programs and our mRNA technology. We intend to leverage the broad applicability of our MRT platform through our collaboration with Sanofi Pasteur Inc., or Sanofi, the vaccines global business unit of Sanofi S.A., to develop infectious disease vaccines using mRNA technology, or mRNA vaccines, for up to five infectious disease pathogens.

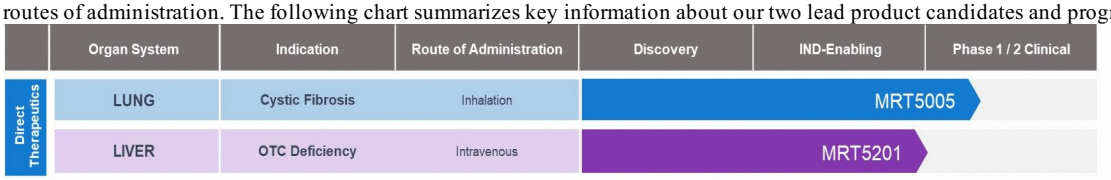
Our technology and products are protected by an extensive intellectual property portfolio, including issued patents and pending patent applications covering mRNA sequences, lipids and polymer composition of matter, manufacturing, specific targets, disease treatments, and formulation and delivery technology. We continue to innovate to improve both the mRNA constructs as well as the delivery technology involved in creating our MRT product candidates.

Going Concern

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $144.1 million. Based on our recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. For a further discussion of our liquidity, please refer to Part II, Item 7 of this report under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Funding Requirements" and Note 1 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K.

Our Pipeline

Our proprietary MRT platform has been designed with the potential to apply across a broad array of diseases and target tissues and through multiple routes of administration. The following chart summarizes key information about our two lead product candidates and programs:



In addition to the programs above, we have several discovery-stage programs focused on treating diseases that potentially can be addressed by delivery of mRNA to the lung, liver, eye, CNS and lymphatic system.

Our Strategy

Our goal is to continue building a leading, global mRNA therapeutics company that capitalizes on our extensive experience with proprietary mRNA product development, delivery, manufacturing and process development. Our proprietary MRT platform has enabled us to focus on direct therapeutic approaches to treat specific genetic diseases with high unmet medical need. We are leveraging our platform's broad applicability and believe that our first-in-class MRT product candidates in CF and OTC deficiency have the potential to transform these debilitating and life-threatening illnesses into manageable chronic conditions with an improved quality of life.

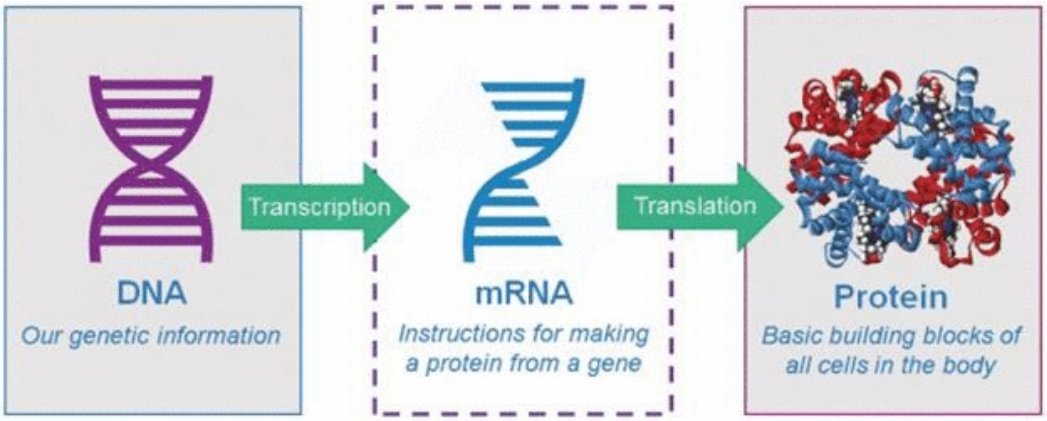
The key components of our strategy to achieve our goal include:

- Rapidly advance MRT5005 through clinical development as a first-in-class treatment to provide mRNA encoding the fully functional CFTR protein in all patients with CF, regardless of the specific genetic mutation, by directly addressing the underlying cause of the disease.

- Rapidly advance MRT5201 into and through clinical development as a first-in-class treatment to provide mRNA encoding the fully functional OTC enzyme in patients with OTC deficiency by directly addressing the underlying cause of the disease.
- Continue research and development activities to advance mRNA vaccines through our collaboration with Sanofi.
- Leverage the broad applicability of our proprietary MRT platform by developing additional MRT product candidates for our own pipeline as well as selectively pursuing strategic collaborations. Specifically, we intend to:
    - Maintain our initial focus on genetic diseases with high unmet medical need in the lungs and liver to utilize our platform to rapidly develop new product candidates targeting these tissues.
    - Broaden our focus to develop product candidates that address diseases with high unmet medical need, including CNS disorders and ocular diseases, or that could be applied to produce therapeutic antibodies and vaccines in areas such as infectious disease and oncology.
    - Explore opportunities to collaborate where potential partners may add strategic value to our platform or programs.
- Develop deep and active relationships with patient advocacy groups in order to better understand the needs of patients to optimize our treatment approaches and also to identify patients that could potentially benefit from our MRT product candidates.
- Seek strategic acquisitions or in-licenses of technology or assets that may complement our proprietary MRT platform and programs.
- Aggressively strengthen and protect our intellectual property and scientific and technical know-how.
- Maintain the flexibility to develop and potentially commercialize products ourselves.

The Role of mRNA

mRNA is a fundamental component of gene expression. It is the key link in the process of translating genetic information encoded in DNA into instructions that are used by cells to produce the proteins needed to carry out essential cellular functions. These instructions are processed through cellular mechanisms in two steps: transcription and translation. During transcription, a gene that encodes an amino acid sequence for a particular protein is transcribed into a complementary sequence of mRNA. The mRNA then carries these instructions to other areas of the cell where the instructions are translated by ribosomes, which are specialized molecular machines within cells that carry out protein synthesis. During transcription, the ribosomes use the instructions conveyed by mRNA as a template for assembling the amino acids to create the desired protein. The following graphic illustrates the transcription and translation processes.



Abnormal gene expression, caused by a mutation in a DNA sequence, can result in the transcription of defective instructions. The translation of defective instructions by the cell can lead to the failure to produce, insufficient production or over production of a protein, or the production of dysfunctional proteins. This protein defect is the underlying cause of genetic disease.

There are several existing treatment approaches that seek to address the underlying cause of the absent or defective proteins associated with genetic disorders, including protein replacement therapy, gene therapy, gene editing and small molecule therapies. However, each has important limitations.

Existing Treatment Approaches and Their Limitations

Protein Replacement Therapy

Protein replacement therapy seeks to supplement or replace absent or deficient proteins or enzymes. While this approach has been used successfully to treat a subset of protein-based disorders, it is most effective if the protein carries out its function outside the cell. However, a majority of genetic disorders involve intracellular or transmembrane proteins, which carry out their function inside the cell. These proteins are significantly more challenging to replace.

Gene Therapy

Gene therapy is the process of introducing a functional copy of a defective gene sequence into a patient's cells to express the desired protein. However, some current gene therapy approaches do not efficiently integrate this functional genetic sequence into the genome, while other approaches randomly integrate thereby causing safety concerns. The failure to efficiently integrate results in the functional genetic sequence not being effectively passed to new cells following cell division. As a result, in genetic disorders that involve dividing cells, such as epithelial cells of the lung, the efficacy of gene therapy may be limited. Repeated gene therapy treatments may be required to effectively treat such disorders. However, the ability to provide repeated treatments is limited by current gene therapy's reliance on the delivery through a viral vector, which is an engineered virus that is designed to express genes of interest and results in serious challenges concerning safety and immunogenicity, such as neutralizing antibodies. The success of this approach is further limited by difficulties in delivering the therapy to the cell nucleus, which is a crucial step to ensure ultimate expression of the desired therapeutic protein. The cost of manufacturing gene therapy product candidates in large scale is also significant.

Gene Editing

Gene editing seeks to permanently replace, delete or repair a defective gene sequence at the natural gene location in a patient's genome. In contrast to gene therapy, an edited genetic sequence would be replicated in new cells following cell division, thereby reducing or eliminating the need for repeat dosing. However, current methods of gene editing face significant limitations, including unwanted on- and off-target modifications to DNA, failure to make the intended modification, challenges in introducing the particular edit into the cell nucleus, and manufacturing complexities. There are currently no approved gene editing products, and there is limited clinical experience with this approach.

Small Molecule Therapy

In small molecule therapy, small molecules are designed to bind to disease-associated molecules and modulate their activity. Small molecule approaches to genetic disorders have limitations, including the inability to directly address specific gene defects and the potential to cause off-target toxicities.

mRNA Therapy

mRNA therapy has long been of interest because of its potential to overcome many of the shortcomings of existing approaches. The goal of mRNA therapy is to provide the instructions needed for cells to produce functional proteins through the cells' own machinery. mRNA does not integrate into or alter the genome, which may offer a better safety profile than gene therapy, gene editing or small molecule therapy. Because mRNA is a natural component of all cells, it is inherently biocompatible. As such, mRNA therapy offers the ability to titrate and dose repeatedly. The central role of mRNA in protein expression confers the potential for mRNA therapy to have broad applicability across multiple diseases in which the production of a desirable protein can have a therapeutic effect.

However, the potential of mRNA therapy has been unrealized due to the following key challenges:

- *Stability*: mRNA is susceptible to rapid degradation by nucleases, including ribonuclease, or RNase, which can limit the duration of the therapeutic effect.

- *Immunogenicity*: An effective therapeutic mRNA must be pure and in a form not recognized by the body as foreign to avoid triggering an immune response.

- *Delivery*: Therapeutic mRNA must be safely and effectively delivered across the cell membranes of the target tissues without off-target toxicity and degradation.

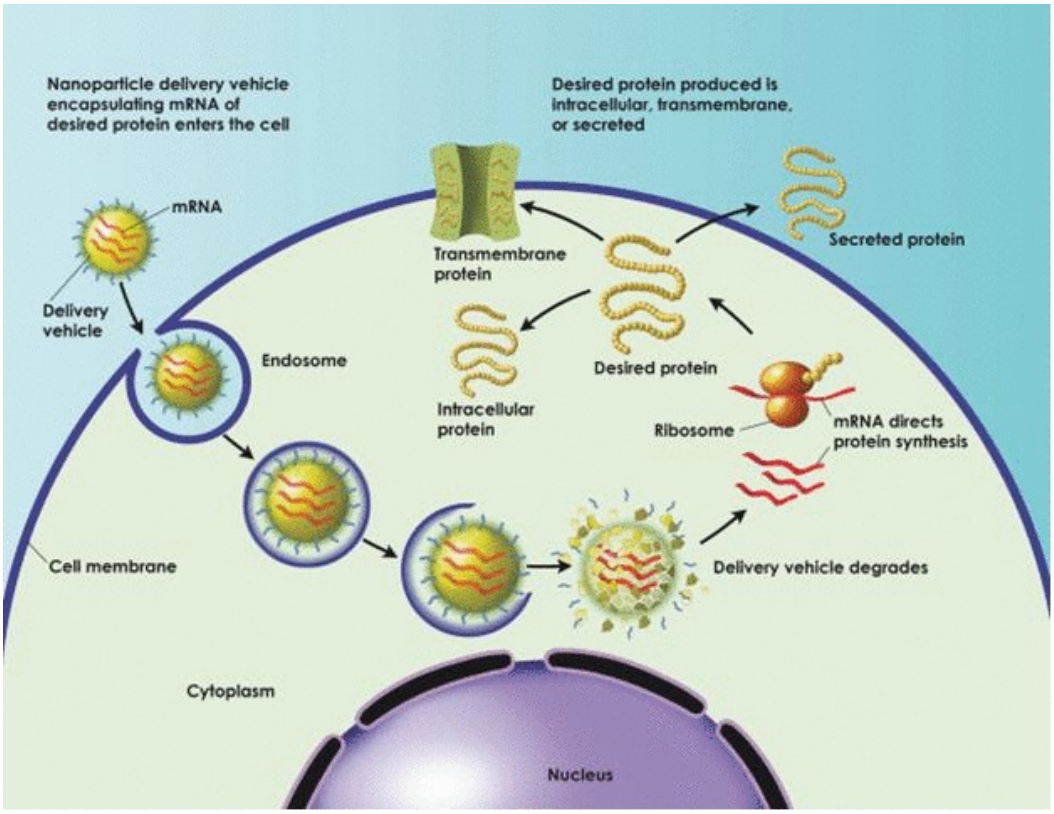
- *Manufacture of mRNA Products*: It is difficult to achieve scalable and cost-effective manufacturing of stable and non-immunogenic therapeutic mRNA in quantities sufficient to support clinical trials and commercial production.

We believe that our scientific expertise and years of investment in mRNA construct design, delivery and manufacturing have allowed us to overcome many challenges that have limited the development of mRNA therapy.

Our MRT Platform

Our MRT platform has enabled us to develop product candidates designed to deliver mRNA that can carry instructions to produce intracellular, transmembrane and secreted proteins. Our platform is also designed to be flexible and scalable by allowing for the development of MRT product candidates that vary only in the mRNA sequence and the tissue-specific delivery vehicle. This modular nature of our platform may allow us to rapidly advance into new indications after successfully establishing delivery vehicles for specific tissues. For example, we are utilizing our MRT platform to identify and rapidly develop new product candidates designed to address the underlying causes of additional diseases of the lung and liver.

As depicted below, mRNA directly provides the instructions for the body to produce proteins. Our MRT product candidates are designed to enter the cell and unpackage our therapeutic mRNA in the cytoplasm. Upon release of the mRNA, the ribosomes in the cell engage the mRNA and begin the translation process, resulting in the production of the desired natural protein. This process of translation is designed to continue until the mRNA is expended.



Advantages of our MRT Platform

We believe that our proprietary MRT platform and the design of our product candidates, which consist of the protein-coding mRNA and a delivery vehicle, will enable us to overcome the challenges of mRNA therapy and allow for chronic dosing of our MRT product candidates for the following reasons:

- *Enhanced Stability*. Our mRNA design, manufacturing processes and nanoparticle formulations are designed to protect our mRNA from degradation by nucleases, including RNase, and by chemical or physical forces, in order to achieve the appropriate duration of therapeutic effect.

- *Targeting Lower Immunogenicity*. We use manufacturing processes to remove impurities and we design our mRNA using structural components that are identical to natural mRNA within the body, thereby potentially reducing the risk of stimulating an immune response.

- *Tissue-Specific Delivery*. Our delivery technology is designed for efficient encapsulation and cellular uptake in target tissues, thereby reducing the risk of degradation, off-target toxicity and unwanted stimulation of the immune system.

- *Scalable and Flexible Manufacturing*. We employ a unique, biosynthetic, cell-free process to manufacture pure, high-quality mRNA and delivery vehicles with significant potency at a scale suitable for clinical trials and that is designed to be scaled to support commercial production.

mRNA Construct Design

Delivering the desired mRNA sequences is the first step to restoring healthy function to proteins. In our preclinical studies, we observed that such mRNA sequences, when flanked by proprietary signaling sequences and packaged into our delivery vehicles, entered cells and restored proper cellular protein production.

We design our proprietary mRNA sequences to encode the natural protein sequences. We use unmodified mRNA bases to replicate the composition and function of endogenous mRNA. We then further optimize the sequences to result in efficient protein production. We achieve this optimization through the selection of appropriate transcription and translational control elements to maximize protein expression across a broad range of tissues.

Delivery

After we create the desired mRNA sequences, we then package our mRNA sequences into delivery vehicles, such as our LNPs, that are customized for delivery to specific tissues. We design our delivery vehicles for optimal size, surface charge and lipid composition.

For example, MRT5005 is intended to address the underlying cause of CF, and thus we use a lipid composition and particle size designed specifically to deliver mRNA to the lung by inhalation. By contrast, MRT5201, which is administered intravenously, is intended to address the underlying cause of OTC deficiency, and thus its lipid composition and particle size are designed specifically to deliver mRNA into hepatocytes.

We intend to apply our delivery expertise gained in the development of our lead MRT product candidates to the design, optimization and manufacturing of new MRT product candidates.

Our LNPs are designed to have low immunogenicity, meaning that they are intended to avoid stimulating the body's natural response to exogenous therapies, thereby preventing the formation of antibodies which can neutralize exogenous therapeutic products and dramatically decrease their efficacy. Neutralizing antibodies pose a major limitation to gene therapies and related approaches. In preclinical studies, we have not observed any neutralizing antibody effect towards our MRT product candidates and have observed continued therapeutic benefits after repeat administrations. Because we can dose our MRT product candidates repeatedly, we expect to be able to titrate dosing to the minimally effective dose to maximize patient-specific therapeutic benefit. The ability to dose repeatedly may also allow us to treat cells that routinely turn over in the body, such as epithelial cells in the lungs.

Manufacturing

Through years of investment, we have established current Good Manufacturing Practices, or cGMP, of our mRNA drug substance. We have developed proprietary processes that reproducibly provide sufficient quantities of highly pure, high-quality and highly potent mRNA to support our clinical trials. We have made extensive efforts to develop analytical assays to allow for complete characterization of the mRNA drug substance. These assays allow us to demonstrate the quality and potency of the resulting mRNA drug substance. We believe that our manufacturing processes successfully address key issues commonly associated with the manufacturing of mRNA, such as poor capping at one end of the mRNA sequence and the extensive presence of prematurely terminated sequences, such as double-stranded RNA and other contaminants.

The modular nature of our mRNA drug substance manufacturing processes allows for versatility by using the same core production and purification processes for any mRNA drug substance. We only change the sequence of the coding region for the desired mRNA candidate to produce a new mRNA drug substance. Further, we believe that our manufacturing process is cost-effective and minimizes development costs associated with a new mRNA drug substance because, unlike other treatment approaches, it does not require new cell line development or a new production and purification process for each new MRT product candidate.

We have also established cGMP manufacturing of the LNP drug product, which is the delivery vehicle containing the mRNA drug substance. We have developed a proprietary process to produce high-quality, highly potent and stable LNPs that encapsulate our mRNA drug substance. We have designed our LNP drug product to facilitate cellular uptake as well as provide stability, including against degradation by nucleases, such as RNase. We have designed a large-scale cGMP manufacturing process for our LNP drug products that we believe can support our clinical trials and is readily scalable. We have made extensive efforts to develop analytical assays to allow for complete characterization of the LNP final drug product and to allow us to demonstrate the quality and potency of the final LNP drug product.

Similar to our mRNA manufacturing, our LNP manufacturing process utilizes a modular approach that we believe will be cost-effective and will minimize development costs associated with each new mRNA drug substance.

Broad Applicability of our MRT Platform

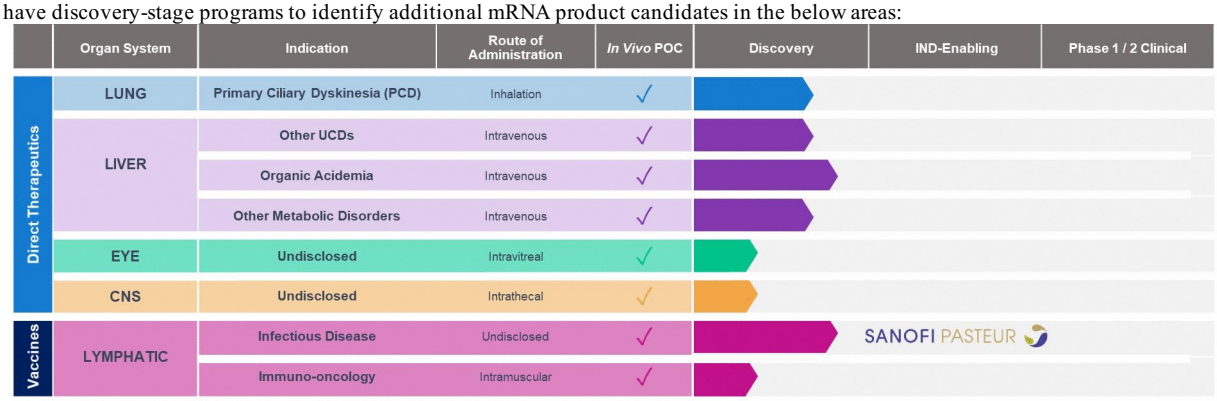
We believe that our MRT platform may be applied across a broad array of diseases and target tissues via multiple routes of administration. In addition to the inhalation and intravenous administration employed for our two lead programs for the treatment of CF and OTC deficiency, respectively, we have observed successful production of the desired proteins through other routes of administration in preclinical studies, which may allow us to develop MRT product candidates for the treatment of a wide range of rare and non-rare diseases, including CNS disorders and ocular diseases. We believe our platform may also be applied to produce therapeutic antibodies and vaccines in areas such as infectious disease and oncology.

We intend to leverage the broad applicability of our MRT platform beyond its current therapeutic applications through the pursuit of strategic collaborations that we expect will enable us to develop our platform in non-core areas. We entered into a collaboration and license agreement with Sanofi to develop mRNA vaccines for up to five infectious disease pathogens. The agreement became effective in July 2018.

Under the agreement, we and Sanofi have agreed to jointly conduct research and development activities to advance mRNA vaccines during a three-year research term, which may be extended by mutual agreement. The agreement provides for Sanofi to make an upfront payment to us of $45.0 million, which we received in July 2018. The agreement provides that we are eligible to receive aggregate potential payments of up to $805.0 million from Sanofi, which includes the $45.0 million upfront payment, certain development, regulatory and sales-related milestone payments across several vaccine targets as well as option exercise payments if Sanofi exercises its options related to development of vaccines for additional pathogens. In addition, we are eligible to receive tiered royalty payments on worldwide net sales of mRNA vaccines. Sanofi is responsible for costs during the research term, and we have granted Sanofi exclusive worldwide commercialization rights. We will be responsible for clinical manufacture and will be entitled to additional payments under a separate supply agreement to be entered into by the parties.

Vaccines work by mimicking disease-causing agents to stimulate the immune system, building up a defense mechanism that can be deployed to fight future infections. mRNA vaccines offer an innovative approach by delivering the nucleotide sequence encoding a protein associated with prevention or treatment of a pathogen. Because of their high potency, capacity for rapid development and potential for low-cost manufacture and safe administration, we believe that mRNA vaccines represent a potentially innovative alternative to conventional vaccine approaches. The same production process to manufacture mRNA designed to create desired protein for our product candidates can be used to manufacture different mRNA for vaccines, which we believe provides flexibility in development and potentially enables the development of vaccines for disease areas where vaccination is not yet a viable option.

We have discovery-stage programs to identify additional mRNA product candidates in the below areas:



Our Programs

Lead Program for the Lung: MRT5005

Our lead MRT product candidate for the lung, MRT5005, is designed to address the underlying cause of CF by delivering mRNA encoding fully functional CFTR protein to the lung epithelial cells through nebulization. In preclinical studies, successful delivery of MRT5005 resulted in the production of fully functional CFTR protein. According to research from the National Institutes of Health, or NIH, the average number of copies of human CFTR mRNA is approximately one or two per cell. We believe that we can provide therapeutic levels of human CFTR mRNA because MRT5005 is designed to efficiently deliver human CFTR mRNA to the lung with widespread distribution.

There is a large unmet medical need in the CF patient population as the currently approved therapies are limited to patients with specific genetic mutations and patients treated with these therapies still suffer from long-term decline in lung function and exacerbations that require hospitalization. MRT5005 has the potential to treat all patients suffering from CF, regardless of the mutations present. Our goal for MRT5005 is to provide patients with significant improvements in lung function, halt the progressive decline in lung function and substantially reduce the frequency of pulmonary exacerbations.

We believe MRT5005 is the first clinical-stage mRNA product candidate designed to deliver mRNA encoding fully functional CFTR protein to lung epithelial cells. We have initiated a double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005 in which we plan to enroll at least 32 patients with CF. In late May 2018, we began enrolling and dosing patients in the single-ascending dose part of this trial. In January 2019, we announced that we received approval from the Protocol Safety Review Committee to initiate the MAD portion of the trial and in February 2019, we announced that dosing of patients in the MAD portion of the trial had begun. We anticipate reporting interim data from the Phase 1/2 clinical trial in the second half of 2019.

Cystic Fibrosis

CF is the most common fatal inherited disease in the United States. CF results in mucus buildup in the lungs, pancreas and other organs, and mortality is primarily driven by a progressive decline in lung function. There is no cure for CF. According to the Cystic Fibrosis Foundation, or CFF, the median age at death for patients with CF in the United States was 30.6 years in 2017. According to the CFF, approximately 30,000 patients in the United States and more than 70,000 patients worldwide are living with CF and approximately 900 new cases of CF are diagnosed each year. Patients with CF experience frequent pulmonary exacerbations, chronic infections and persistent inflammation, all of which may require outpatient doctor visits and hospitalizations. In some severe cases, these patients require lung transplants. The quality of life for patients with CF is severely compromised and requires significant self-care time, including life-long treatment with multiple daily medications, use of nebulizers and physiotherapy.

CF is caused by dysfunctional or missing CFTR protein. The CFTR protein functions as a channel that regulates the movement of chloride ions in and out of the cells of organs such as the lungs, pancreas and the gastrointestinal tract. Through regulation of these ions, the amount of salts in the fluid both inside and outside of the cell remains balanced. When CFTR protein expels the ions, water is drawn out of cells and hydrates the cell surface. In patients with CF, the CFTR protein is defective and cannot perform its normal function of transporting ions across the cell membrane, resulting in an environment characterized by thick mucus on affected cellular

surfaces. The deficiency in CFTR protein activity in patients with CF is particularly problematic in the lungs, where the build-up of thick mucus obstructs air flow and provides a favorable environment for bacteria, which leads to chronic infection and persistent inflammation.

Current Treatment Landscape for CF

Until the development of CFTR modulators, approved therapies to treat patients with CF only treated the symptoms of CF, by preventing and controlling infections that occur in the lungs. Accordingly, antibiotics are frequently used in conjunction with mucus-thinning drugs. A significant portion of patients with CF are prescribed bronchodilators, although no bronchodilator is currently approved by the FDA for the treatment of patients with CF.

For patients with certain genetic mutations, three medications have been shown to have direct effects on CFTR. The first is ivacaftor, or Kalydeco, a small molecule marketed by Vertex Pharmaceuticals Inc., or Vertex, which stimulates the activity of certain types of defective CFTR and is known as a CFTR potentiator. Another CFTR-specific drug, lumacaftor, helps stabilize defective and misfolded CFTR molecules, allowing increased trafficking of CFTR to the cell membrane rather than to protein degradation pathways. Orkambi, a small molecule also marketed by Vertex, combines ivacaftor and lumacaftor. Orkambi was approved by the FDA in 2015 based on its ability to improve lung function in subsets of patients with CF with certain genetic mutations. A third drug marketed by Vertex, tezacaftor/ivacaftor and ivacaftor, or Symdeko, was approved in February 2018 by the FDA for the treatment of patients with CF who are homozygous for the F508del mutation in the CFTR gene or have at least one mutation in their CFTR gene that is responsive to tezacaftor/ivacaftor. Vertex reported aggregate product revenues of $3.04 billion from sales of Kalydeco, Orkambi and Symdeko in 2018 and $2.17 billion from sales of Kalydeco and Orkambi in 2017. While these therapies improve lung function, they are limited to patients with certain genetic mutations, and although Kalydeco is considered the best available treatment for providing clinical benefit in pulmonary function in CF, patients treated with Kalydeco still experience pulmonary exacerbations, which are typically caused by bacterial infections in the lungs. None of Kalydeco, Orkambi or Symdeko is able to halt the progressive decline in pulmonary function, which represents a significant unmet medical need.

An mRNA therapy that results in the expression of the functional CFTR protein has the potential to significantly reduce the number of pulmonary exacerbations, halt the progressive decline in pulmonary function and provide significant improvements in lung function. We believe there is a significant unmet need and market opportunity for an mRNA therapy that can restore fully functional CFTR protein across all patients with CF regardless of the underlying genetic mutation.

Our Solution: MRT5005

We are developing MRT5005 to treat all patients with CF, regardless of the underlying mutation in CFTR, including those with limited or no CFTR protein. We designed MRT5005 to be inhaled via a handheld nebulizer. Once the inhaled MRT5005 has entered the epithelial cells lining the patient's lungs, our therapeutic mRNA uses the cells' own machinery for translation and expression of fully functional CFTR protein, thereby restoring this essential ion channel, which we believe will address the pathology of CF directly. Our CFTR mRNA encodes the protein that forms a functional ion channel that is defective or absent in patients with CF, and we have observed functionally active ion channels in preclinical studies. In our preclinical studies we have observed dose-dependent increases in CFTR being restored to cell membranes. The inhaled formulation of MRT5005 resulted in broad CFTR expression in lung tissue. We are conducting a Phase 1/2 clinical trial to evaluate the safety and efficacy of MRT5005 in patients with CF.

Phase 1/2 Clinical Trial. In our double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005, we plan to enroll at least 32 adult patients with CF across multiple sites in the United States. In Part A of the clinical trial, three groups of four subjects each will receive a single dose of placebo or 8 mg, 16 mg or 24 mg of MRT5005, respectively. In Part B of the trial, different subjects will receive five weekly doses of placebo or 8 mg, 16 mg or 24 mg of MRT5005. In Part C of the trial, the final part, two groups of four subjects each will also receive five weekly doses of placebo or one of the two highest tolerated doses, and will also undergo bronchoscopies prior to the first dose and after the last dose. The primary endpoint of this trial will be the safety and tolerability of MRT5005. Secondary endpoints will include quantitative measures of the ability to deliver CFTR mRNA and show expression of CFTR protein in bronchial cells retrieved from patients' airways and to assess changes in CFTR ion channel activity in the airways.

In this Phase 1/2 clinical trial, we will also perform measurements of forced expiratory volume in one second, or FEV1, which is a well-defined and accepted endpoint measuring lung function based on completed clinical trials for currently marketed therapies. FEV1 represents the amount of air that can be exhaled from the lungs in one second. The rate of decline in FEV1 in patients with CF has been demonstrated to correlate with life expectancy and to be a strong clinical predictor of mortality. In patients with CF, lung function is typically reported as a fraction of their FEV1 compared to that of a healthy individual of the same height, sex and race. We expect to design future clinical trials in which improvements in FEV1 or the reduction of pulmonary exacerbations will be the primary efficacy endpoint.

We anticipate reporting interim data from the Phase 1/2 clinical trial in the second half of 2019.

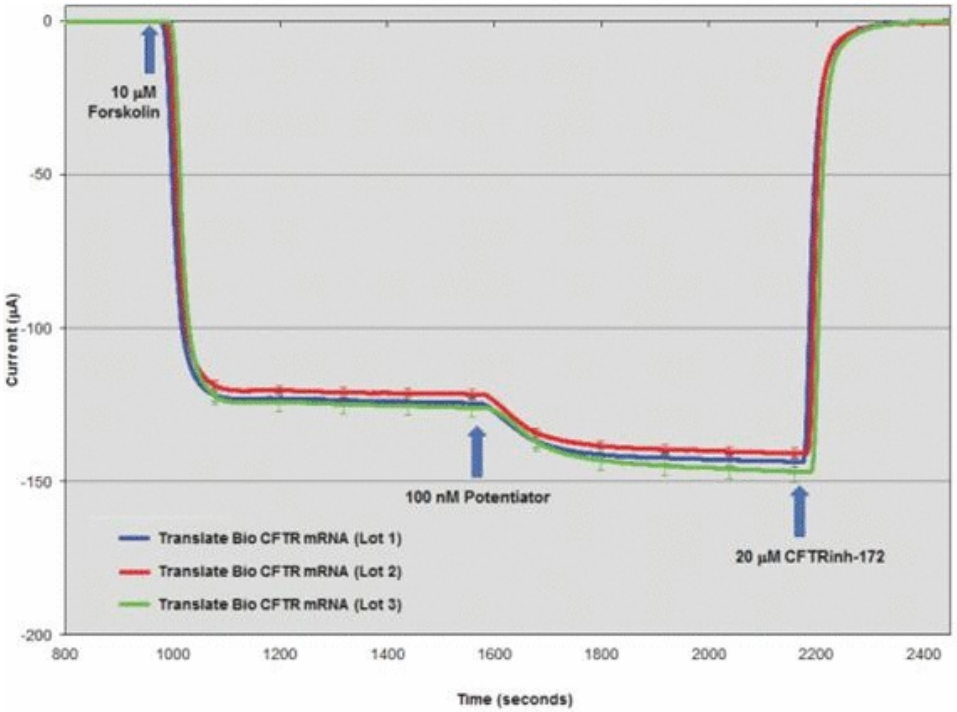
Preclinical Validation of Our Approach. Human CFTR protein is a large, transmembrane protein that undergoes critical folding and extensive glycosylation prior to being trafficked to incorporate into the membrane of the cell within the lungs. By delivering mRNA encoding the CFTR protein to cells, we rely on the endogenous ribosomes to not only translate the proper CFTR protein, but also to accurately fold, glycosylate and traffic the protein to its natural state and location within the cell.

Our preclinical program included *in vitro* studies as well as *in vivo* studies in multiple species to establish the ability of our MRT platform for the treatment of CF. We conducted *in vitro* studies in which we observed that our CFTR mRNA drug substance successfully resulted in the production of human CFTR protein and we observed ion channel activity of the measured CFTR protein. We obtained substantial data through *in vivo* studies conducted in mice, rats and non-human primates, or NHPs. In these studies, we observed successful mRNA delivery and subsequent human CFTR protein production within the lungs of all species tested. In addition, we generated ion channel activity, biodistribution, pharmacokinetic and safety data through *in vivo* evaluation of single- and multiple-dose regimens.

In Vitro Validation of MRT5005. We performed an *in vitro* study to evaluate the ability of our CFTR mRNA drug substance to produce human CFTR protein. In this study, we introduced the mRNA into cells and, after a given period of time, we analyzed the cells for human CFTR protein using standard laboratory methods. We observed a dose-dependent correlation with respect to both the amount of CFTR mRNA introduced into cells and the amount of full length human CFTR protein produced.

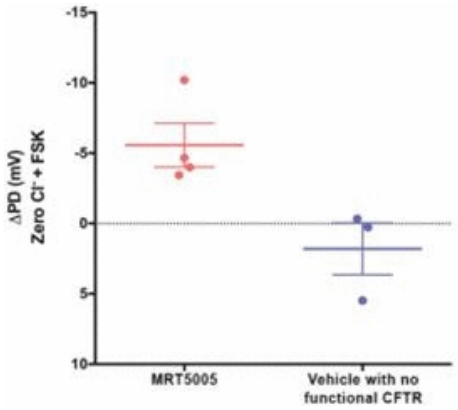
Once we established that our mRNA drug substance could produce the desired human CFTR protein, we used an *in vitro* Ussing Chamber assay to evaluate whether the mRNA-derived CFTR protein was active. An Ussing Chamber assay is commonly used to determine the function of CFTR protein by measuring ion transport across a cell membrane through CFTR. In this *in vitro* study, we evaluated the activity of the CFTR protein that was produced from three separate manufacturing lots of our CFTR mRNA drug substance. We evaluated each lot of our CFTR mRNA in polarized epithelial cells and conducted electrophysiological assays to measure ion flow across the cell membrane through our CFTR mRNA.

As depicted below, three independent parameters confirmed that this ion flow was due to increased CFTR activity. First, the activity was stimulated by forskolin, a known activator of CFTR. The activity was further stimulated by ivacaftor, an FDA-approved potentiator of CFTR function, and it was selectively inhibited by a human-specific CFTR inhibitor. Based on these findings, we believe that the human CFTR protein produced from our mRNA drug substance was active and produced normal ion channel activity.



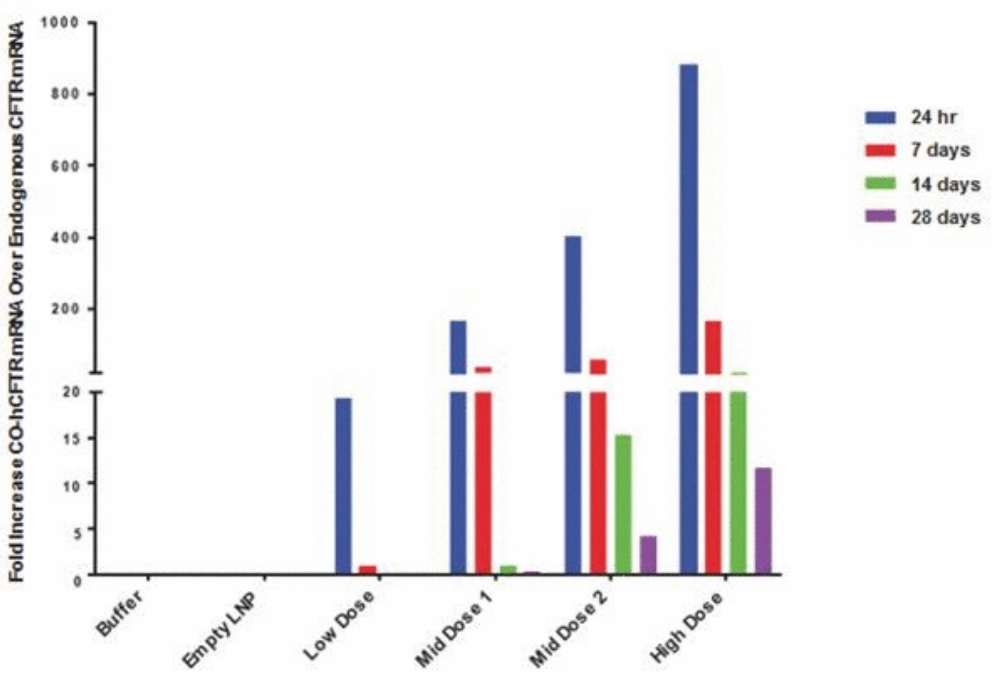
Additionally, in other *in vitro* studies, MRT5005 demonstrated active CFTR ion channel in human bronchial epithelial cells that were derived from human lung tissue.

In Vivo Validation of MRT5005. We conducted *in vivo* studies to further evaluate whether the application of MRT5005 produced fully functional CFTR protein activity. In order for the mRNA drug substance to enter the epithelial cells, MRT5005 must cross the mucus layer of the diseased lung. We tested MRT5005 in a rat CFTR knockout model developed at the University of Alabama. The rats in this model had increased mucus occlusions within the lung layer and nasal epithelial cells, which resemble conditions comparable to those of humans with CF. We evaluated the ability of MRT5005 to cross the mucus layer of diseased cells and produce functional CFTR protein in the underlying epithelial cells by measuring forskolin-induced electrochemical changes in respiratory epithelial cells of anesthetized rats. In this study, the lack of functional CFTR ion channel activity resulted in a potential difference change of approximately five millivolts. These data support the ability of MRT5005 to cross the mucus layer of diseased cells and deliver our CFTR mRNA to the underlying cells thereby resulting in the production of functional CFTR proteins in the cells. The figure below depicts the potential difference in the forskolin-induced electrochemical changes in rat respiratory nasal cells with and without CFTR-dependent chloride transport in the rat CF model after treatment with MRT5005.



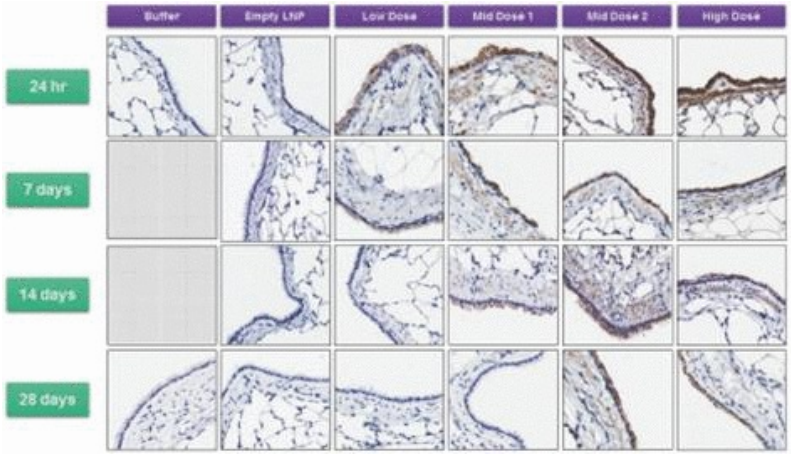
We also investigated the ability of a single dose of MRT5005 to deliver CFTR mRNA to lungs in rats and NHPs. We observed CFTR mRNA levels of up to 1,500-fold higher than normal in NHPs 24 hours after a single exposure to MRT5005. We also observed high levels of human CFTR mRNA deposition after a single administration in rats. While these levels in the rats decreased over time, CFTR mRNA deposition was still detectable at higher than normal levels 28 days after administration at the highest doses. Biodistribution analysis of multiple respiratory tract organs demonstrated that the large majority of our drug product deposited in the lungs of rats and NHPs. We believe that these results provide preclinical validation of the ability of MRT5005 to reach the lungs while protecting the delivered mRNA from rapid degradation by nuclease activity.

The figure below presents the fold increase in levels of human CFTR mRNA in the lungs of rats after a single aerosolized administration of MRT5005 when compared to normal rat CFTR mRNA levels.

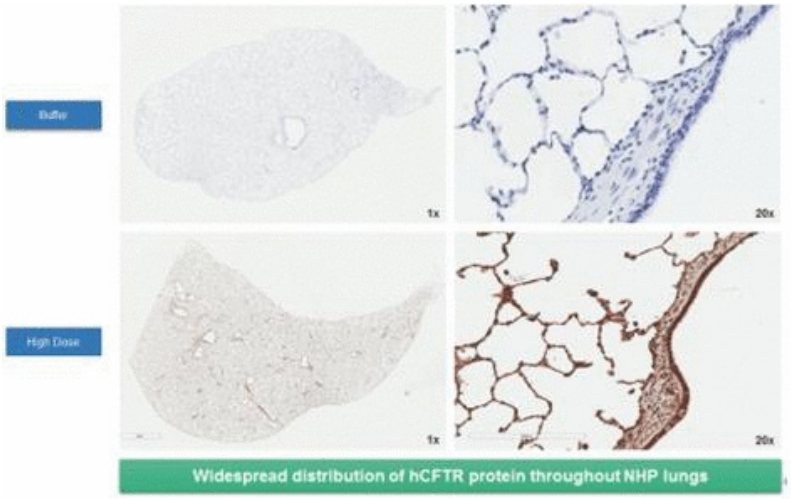


We evaluated CFTR protein expression in normal NHPs and rats and observed a dose-dependent staining intensity that generally reflected the mRNA levels that were measured. Importantly, after a single dose, we observed significant staining in the NHPs at one week post-administration. We observed remaining CFTR expression at 28 days post-administration at the high dose levels in the rats. We observed that CFTR protein expression was widespread throughout the upper and lower airways in both NHPs and rats.

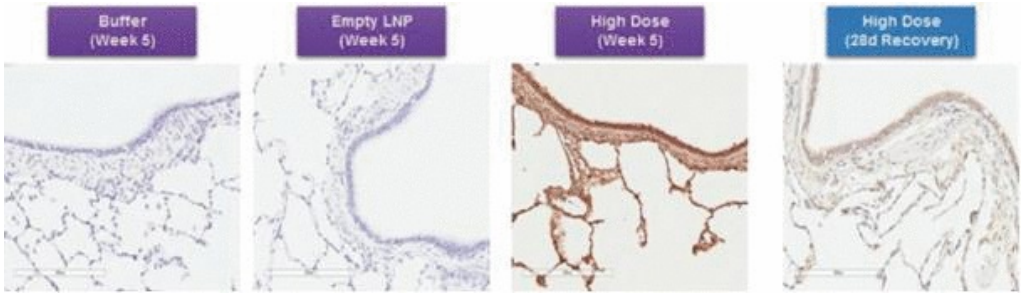
In this study, and as shown in the figure that follows, we observed that cells throughout the bronchial and alveolar epithelium demonstrated dose-dependent CFTR protein expression.



The figure below shows widespread distribution of human CFTR protein in lung tissue with successful human CFTR protein production in both bronchial epithelial cells as well as alveolar regions in NHPs. We have also observed membrane localization of human CFTR protein within the lung epithelial cells of treated NHPs.



We have conducted multiple-dose inhalation *in vivo* studies in both rats and NHPs. We administered five weekly treatments with a 28-day recovery period in each species. We monitored safety as well as pharmacodynamic parameters. We observed robust delivery of human CFTR mRNA upon treatment with MRT5005, resulting in higher than normal levels of CFTR mRNA, similar to what we observed in the single dose administration studies. We observed widespread distribution of the resulting human CFTR protein, with intense staining in both the bronchial epithelial cells as well as lower airway and alveolar regions. Upon multiple exposures, we observed the presence of human CFTR protein 28 days after the final treatment in rats and NHPs. More specifically, after five weekly doses of MRT5005, we observed a dose-dependent increase in human CFTR protein production. Data from the multiple-dose study in NHPs is depicted below, representing robust protein production of the high dose at week 5 as well as the presence of human CFTR protein at 28 days post-treatment.



MRT5005 was well-tolerated in all of our preclinical studies at all doses. We have not observed adverse effects or physiological changes throughout the preclinical toxicology studies in rats and NHPs. Histopathological analysis of the lungs and respiratory tract tissues after multiple-dose regimens demonstrated normal histology and normal morphology with no signs of inflammation. Based on these results, we believe that MRT5005 has the potential to safely and efficiently deliver mRNA to the lungs and successfully result in CFTR protein production within the epithelial cells of the lung.

Lead Program for the Liver: MRT5201

Our lead MRT product candidate for the liver, MRT5201, is designed to address the underlying cause of OTC deficiency by delivering mRNA encoding fully functional OTC enzyme to hepatocytes through intravenous administration. There is a large unmet medical need for patients with OTC deficiency as these patients may experience high blood ammonia levels and liver failure and have early mortality. In our preclinical studies, we observed successful delivery of MRT5201 to the liver and the resulting production of fully functional OTC enzyme.

We believe MRT5201 will be the first clinical-stage mRNA product candidate designed to deliver mRNA encoding fully functional OTC enzyme to hepatocytes. Our planned Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency is not yet active and has not recruited any patients. In December 2018, we submitted an IND to the FDA supporting the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Subsequently, the FDA notified us that our IND for MRT5201 was placed on clinical hold. Prior to initiation of our planned Phase 1/2 clinical trial, the FDA is requiring additional preclinical toxicology data to assess the potential for adverse effects related to the clearance time of MRT5201. We have identified the additional preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019.

OTC Deficiency

OTC deficiency is a metabolic liver enzyme disorder that results from a mutation in the OTC gene. OTC deficiency is the most common urea cycle disorder. The OTC enzyme is necessary for preventing the accumulation of ammonia, a normal byproduct of protein breakdown. When the enzyme is defective or absent, high levels of ammonia accumulate in the blood, which can cause serious and irreversible neurological damage.

OTC deficiency can manifest in a neonatal onset form and a later onset form. In the neonatal form, infants with a urea cycle disorder may have symptoms such as lethargy, poor feeding, seizures and breathing difficulties. Unless treatment is promptly initiated, the high ammonia levels, or hyperammonemia, may lead to coma and/or permanent neurocognitive damage. In the later onset form, symptoms may manifest for the first time anytime from childhood to adulthood. These symptoms can include vomiting, developmental delays and seizures. Hyperammonemic crises are often triggered by infections or catabolic-stress.

Based on published research, the incidence of OTC deficiency is estimated to be 1 in 56,500 live births in the United States. OTC deficiency is an X-chromosome-linked disease, and females are typically less severely affected than males.

Current Treatment Landscape for OTC Deficiency

The standard treatment for patients with OTC deficiency consists of severe dietary protein restriction with essential amino acid supplements, along with treatment with ammonia scavengers that drive the incorporation of ammonia into metabolites that are readily excreted. Patients routinely receive carbohydrate- and lipid-rich nutrition, including overnight feeding through a nasogastric tube. During acute hyperammonemic crises, patients with OTC deficiency may require dialysis or hemofiltration to control ammonia levels.

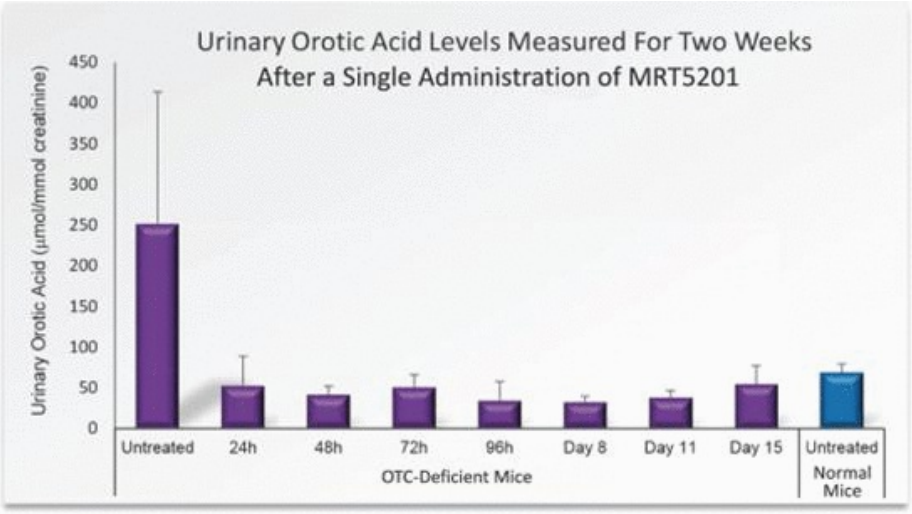
A liver transplant can be a curative solution to OTC deficiency. Liver transplant is limited by donor availability and patient eligibility and has significant risks associated with the surgery. Liver transplantation is especially complicated in neonatal patients and young children, which leads to delaying transplants until these patients are older. Unfortunately, some patients die while awaiting transplants. In addition to these risks associated with surgery itself, transplant patients also frequently suffer long-term complications related to the immunosuppression medications required to prevent organ rejection, which have side effects that include increased rates of infections, malignancy, and kidney toxicity.

Our Solution: MRT5201

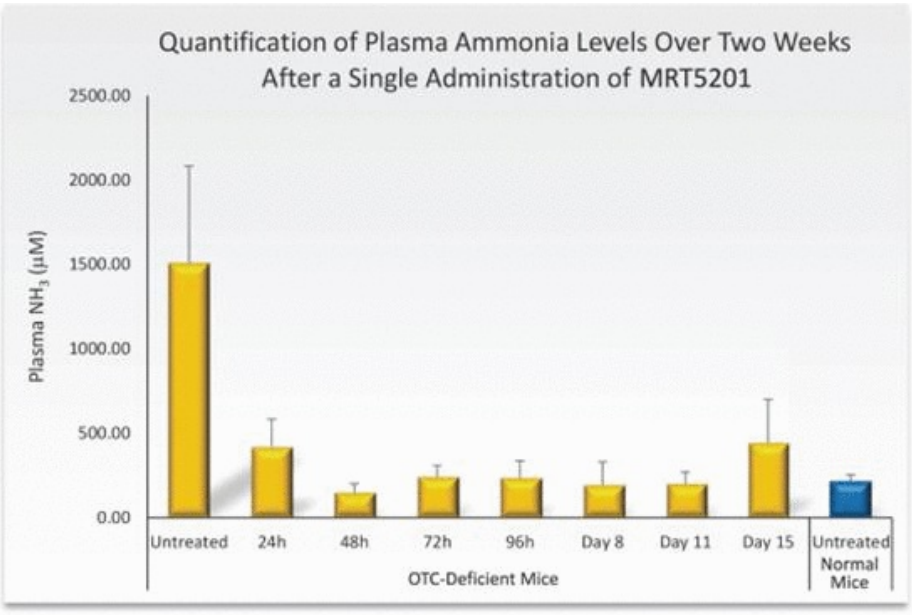
We are developing MRT5201 to treat patients with OTC deficiency. We have developed MRT5201 for intravenous administration and delivery of mRNA encoding fully functional OTC enzyme to the liver to enable the hepatocytes to produce the normal OTC enzyme. We expect that sufficient expression of the natural OTC enzyme in hepatocytes would reduce or eliminate the need for current treatments such as strict low-protein diets or ammonia scavengers. Given the high unmet need and limited therapeutic options available, we believe that regulatory approval can be obtained based on clinical trials with relatively small patient populations. In December 2018, we submitted an IND to the FDA supporting the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Subsequently, the FDA notified us that our IND for MRT5201 was placed on clinical hold. Prior to initiation of our planned Phase 1/2 clinical trial, the FDA is requiring additional preclinical toxicology data to assess the potential for adverse effects related to the clearance time of MRT5201. We have identified the additional preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019.

Preclinical Studies of Our Approach. We have established the ability of our MRT platform to treat OTC deficiency using *in vitro* studies as well as *in vivo* studies in multiple species. We conducted *in vitro* studies demonstrating that our mRNA successfully resulted in the production of human OTC enzyme, as well as subsequent activity of the measured OTC enzyme. We obtained substantial data through *in vivo* studies conducted in mice and NHPs. In these studies, we observed successful mRNA delivery and subsequent human OTC enzyme production within the livers of all species tested. In addition, we evaluated OTC enzyme activity and the biodistribution, pharmacokinetics, efficacy and safety of single- and multiple-dose regimens.

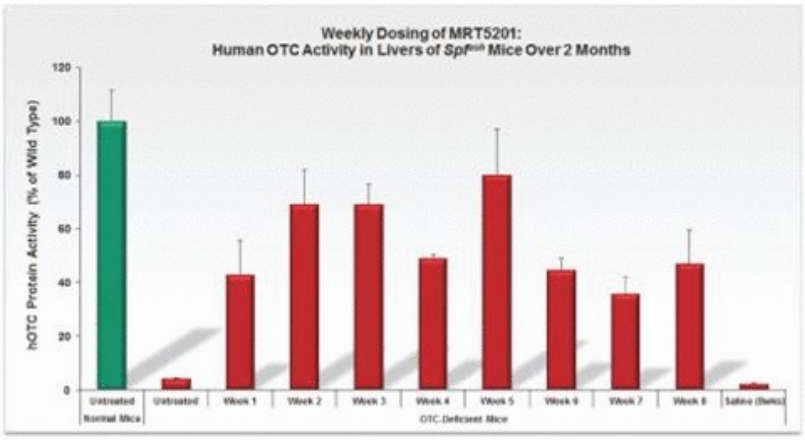
In Vivo Validation of MRT5201. In *in vivo* studies using a mouse model where the gene for OTC has been rendered dysfunctional, we observed delivery of MRT5201 and the resulting expression of functionally active human OTC enzyme. This mouse model was designed to replicate certain clinical features of OTC deficiency, such as elevated urinary orotic acid and the inability to metabolize high levels of ammonia in the blood. As depicted in the figure below, a single treatment with MRT5201 resulted in normalization of urinary orotic acid levels in this mouse model.



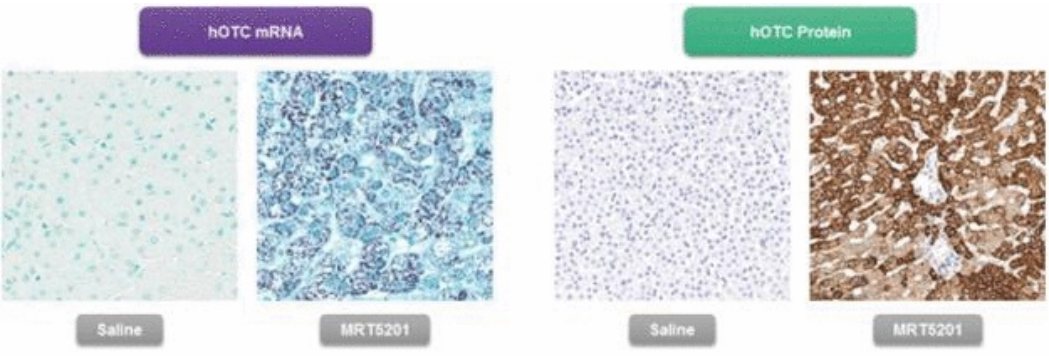
We deliberately challenged OTC-deficient mice with exogenous ammonia to mimic a hyperammonemic episode. Untreated OTC-deficient mice challenged with exongenous ammonia are unable to reduce their ammonia levels and suffer severe morbidity. We observed that after treatment with MRT5201 these OTC-deficient mice were able to reduce their ammonia levels to levels that are normal for wild-type mice, as shown in the figure below. We observed that this protective effect against hyperammonemia persisted in these mice for up to four weeks after a single dose.



We also conducted multiple-dose studies of MRT5201 in OTC-deficient mice. We observed successful OTC enzyme production in the livers of these mice over the course of eight weekly intravenous administrations of MRT5201. We observed robust activity each week resulting in ornithine metabolism levels well above the minimum therapeutic level necessary, which suggested that the OTC enzyme was fully functioning.



An mRNA therapeutic for OTC deficiency must be delivered to a broad population of the liver cells in order to be effective. We conducted *in vivo* studies to evaluate the delivery and distribution of MRT5201 in NHPs. As shown in the figure below, we have observed successful delivery of MRT5201 to the liver, and more specifically to the hepatocytes, of NHPs after intravenous administration. As shown on the left, intracellular mRNA localization after a single dose of MRT5201 in NHPs resulted in the detection of high levels of OTC mRNA throughout the liver, indicating high and widespread distribution. Moreover, as shown on the right, we observed corresponding human OTC enzyme production within the liver cells after treatment with MRT5201.



We have also performed multiple-dose *in vivo* studies of MRT5201 in both mice and NHPs. Based on the studies discussed above, we have established satisfactory therapeutic index levels of MRT5201 in both species, which has enabled us to submit an IND to the FDA to support the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Our planned Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency is not yet active and has not recruited any patients. In response to the FDA's clinical hold on our IND for MRT5201, we have identified the preclinical studies required and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019.

Other Indications and Target Tissues

We believe that our MRT platform may be applied across a broad array of diseases and target tissues via multiple routes of administration, including for the treatment of a wide range of rare and non-rare diseases, including CNS disorders and ocular diseases. We believe our platform may also be applied to produce therapeutic antibodies and vaccines in such areas as infectious disease and oncology.

We have several discovery-stage programs to identify additional potential mRNA therapeutic candidates. Specifically, we are exploring potential MRT product candidates for diseases of the CNS. With regard to MRT product candidates designed to engage the lymphatic system, we are exploring multiple routes of administration, along with conducting research to identify product candidates

for infectious disease and cancer vaccines. Our research for targeted tissues such as the eye, CNS and lymphatic system builds on the preliminary formulations we have identified as well as developing new delivery systems specifically designed for each formulation. We are working to develop new product candidates using our current delivery vehicles to treat additional rare diseases of the lung, including primary ciliary dyskinesia, and the liver. All of these programs are in the discovery stage.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe we have significant competitive advantages with our industry-leading expertise in mRNA technology, rare disease clinical development expertise and advanced intellectual property position, we currently face and will continue to face competition for our development programs from companies that use mRNA, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecules.

The competition is likely to come from multiple sources, including larger pharmaceutical companies, biotechnology companies and academia. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, we will have to compete with new therapies that may become available in the future.

Our competitors also include companies that are or will be developing other mRNA technology methods as well as small molecules, biologics and nucleic acid-based therapies for the same indications that we are targeting with our mRNA-based therapeutics. Some of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. These same competitors may invent technology that competes with our product candidates.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even greater concentration of resources among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and registering subjects for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, health-economic benefit, convenience of administration and delivery, price, the level of generic or biosimilar competition and the availability of adequate reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products faster or earlier than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that our products, if approved, will be priced at a premium over competitive generic products, and our ability to compete may be affected by insurers or other third-party payors encouraging the use of generic products.

mRNA Platform

Companies with mRNA platform capabilities include: Novartis AG, GlaxoSmithKline plc, Moderna, Inc., CureVac AG, BioNTech AG, Ethris GmbH, Arcturus Therapeutics Ltd., eTheRNA immunotherapies NV, Novellus Inc., TranscriptTX, Inc. and Genevant Sciences Ltd.

MRT5005 / Cystic Fibrosis

If approved for the treatment of CF, MRT5005 would compete with Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor) and Symdeko (tezavaftor/ivacaftor and ivacaftor), each of which is marketed by Vertex Pharmaceuticals Incorporated, or Vertex. Vertex also has several CFTR corrector compounds in clinical development, including VX-659, VX-445, VX-440, VX-152, VX-371 and VX-561, each of which is currently in a Phase 2 or Phase 3 clinical trial.

We are aware of several companies with product candidates for the treatment of CF in Phase 2 clinical development in addition to Vertex, including AbbVie Inc., Corbus Pharmaceuticals, Inc., Flatley Discovery Lab, LLC, Laurent Pharmaceuticals, Inc., Novotersis LLC, Protalix BioTherapeutics, Inc., Proteostasis Therapeutics, Inc., Spyryx Biosciences, Inc. and Verona Pharma plc. We are aware of several companies with product candidates for the treatment of CF in Phase 1 clinical development, including AbbVie, Inc., Alaxia SAS, AstraZeneca plc, Boehringer Ingelheim GmbH, Chiesi Farmaceutici S.p.A., Eloxx Pharmaceuticals Ltd, Flatley Discovery Lab, LLC, Ionis Pharmaceuticals, Inc., Paranta Biosciences Ltd, ProQR Therapeutics N.V. and Proteostasis Therapeutics, Inc.

Other companies developing products that modulate or affect CFTR function for the treatment of CF also include: CRISPR Therapeutics AG, Editas Medicine Inc., Ethris GmbH, Moderna, Inc. and Oxford BioMedica plc.

MRT5201 / OTC Deficiency

There are currently no approved therapies that address the underlying cause of OTC deficiency. There are several ammonia scavengers that treat OTC deficiency, including Buphenyl and Ravicti, each marketed by Horizon Pharma plc, and Ammonul, marketed by Swedish Ophan Biovitrum AB and Bausch Health Companies Inc. We are aware of several product candidates in clinical development for the treatment of OTC deficiency that may compete with MRT5201. DTX is an adeno-associated virus, or AAV, OTC gene stimulator in Phase 2 clinical development by Ultragenyx Pharmaceutical Inc. Synlogic, Inc. has a candidate, SYNB1020, in a Phase 1b/2a clinical trial that may relate to the treatment of liver disease with hyperammonemia. HepaStem/Heparesc is a liver progenitor cell-based therapy in Phase 2 clinical development by Promethera Biosciences S.A. Lunar-OTC is an OTC gene stimulator in preclinical development by Arcturus Therapeutics Ltd. SEL-313 is an AAV-based gene therapy in preclinical development by Selecta Biosciences, Inc. in collaboration with Genetheon S.A.

Other companies developing products that modulate or affect OTC function for the treatment of OTC deficiency include Ultragenyx Pharmaceutical Inc., Selecta Biosciences, Inc., Arcturus Therapeutics Ltd. and Synlogic, Inc.

Asset Purchase Agreement with Shire

On December 22, 2016, we entered into an asset purchase agreement with Shire, which, as amended on June 7, 2018, we refer to as the Shire Agreement, pursuant to which Shire assigned to us all of its rights to certain patent rights, permits, real property leases, contracts, regulatory documentation, books and records, and materials related to Shire's mRNA therapy platform, or the MRT Program, including its CFTR and OTC deficiency mRNA therapy programs. The scientific founders of the MRT platform who were responsible for the research, development, manufacturing and delivery know-how and intellectual property supporting this platform joined our company as part of the acquisition. We paid Shire an aggregate purchase price of $112.2 million, consisting of 5,815,560 shares of common stock with an aggregate fair value of $41.1 million on the acquisition date and contingent consideration with an aggregate fair value of $71.1 million on the acquisition date. As further described below, the contingent consideration includes the obligation to issue additional shares of common stock to Shire in connection with the closing of subsequent equity financings required under the terms of the Shire Agreement, as well as the obligation to make future milestone and earnout payments upon the occurrence of specified commercial milestones. We and Shire entered into an amendment to the asset purchase agreement on June 7, 2018 to align certain terms of the asset purchase agreement with the collaboration and license agreement that we entered into with Sanofi on June 8, 2018.

Under the Shire Agreement, we are obligated to use commercially reasonable efforts to develop and seek and obtain regulatory approval for products that include or are composed of MRT compounds covered by or derived from patent rights or know-how acquired from Shire, or MRT Products, and to achieve specific developmental milestones. Pursuant to the amendment entered into on June 7, 2018, an mRNA vaccine that is developed pursuant to our collaboration with Sanofi will be considered an MRT Product if it includes an MRT compound having an mRNA sequence that encodes a protein that is from, or that binds to, an infectious disease pathogen in a field that has been licensed by us to Sanofi. During the earnout period described below, with respect to any MRT Product in any country, we are obligated to use commercially reasonable efforts to market and sell such MRT Product in such country.

We are obligated to make milestone payments to Shire of up to $60.0 million in the aggregate upon the occurrence of specified commercial milestones, including upon the first commercial sale of an MRT Product for the treatment of CF and upon the achievement of a specified level of annual net sales with respect to an MRT Product. We are also obligated to make additional milestone payments of $10.0 million for each non-CF MRT Product upon the first commercial sale of a non-CF MRT Product; provided that such milestone payments will only be due once for any two non-CF MRT Products that contain the same MRT compounds or once per non-CF MRT Product that is a vaccine developed under our collaboration with Sanofi.

Under the Shire Agreement we are also obligated to pay a quarterly earnout payment of a mid-single-digit percentage of net sales of each MRT Product. The earnout period, which is determined on a product-by-product and country-by-country basis, will begin on the date of the first commercial sale of such MRT Product in such country and will end on the later of (i) 10 years after such first commercial sale and (ii) the expiration of the last valid claim of the patent rights acquired from Shire or derived from patent rights or know-how acquired from Shire covering such MRT Product in such country.

Prior to first dosing of the first patient with a CFTR MRT Product in a Phase 3 clinical trial, we are obligated to notify Shire if we receive a written notice from a third party seeking to (i) acquire, license or obtain rights to develop or sell a CFTR MRT Product or (ii) other than a transaction resulting in a change of control of our company, acquire all or a substantial portion of the assets we acquired from Shire or our other assets that are necessary for or related to the development and commercialization of CFTR MRT Products. Before we may enter into negotiations with any third party, Shire has 30 days to notify us of its interest in negotiating an agreement with respect to the rights or assets proposed to be acquired by the third party. If Shire provides such notice, we must negotiate exclusively with Shire for up to 90 days. If Shire does not notify us of its interest in such opportunity within such 30-day period, or if we and Shire do not enter into an agreement with respect to such opportunity within such 90-day period, then, for a period of 12 months, we may grant the rights or sell the assets to a third party on such terms as we may determine in our sole discretion without any further obligation to Shire with respect to the rights or assets subject to the proposal, but we may not enter into exclusive negotiations with any third party for a period longer than 90 days.

Under the Shire Agreement, we were obligated to consummate an equity financing at or prior to the closing of the Shire transaction with gross proceeds of at least $50.0 million, and, because the gross proceeds for our first tranche of such equity financing were less than $100.0 million, we were obligated to use the first $50.0 million of net proceeds solely for activities and expenses associated with the MRT platform and/or specified transferred assets and to satisfy our obligations under the Shire Agreement and related documents until the earlier of (i) the consummation of another tranche or tranches of equity financing with aggregate gross proceeds equal to at least (A) $100.0 million minus (B) the gross proceeds from the first tranche and (ii) full utilization of the proceeds. In addition, we were required to use commercially reasonable efforts to consummate subsequent tranches until aggregate proceeds from the first tranche and all subsequent tranches were at least $100.0 million and, until we completed such equity financings, to issue additional shares of our common stock to Shire in satisfaction of anti-dilution obligations. Our obligation to issue additional shares of our common stock to Shire was satisfied upon the completion of our initial public offering, or IPO.

Pursuant to the Shire Agreement, we may not take any action that would result in Shire and its affiliates beneficially owning more than 19.9% of the voting power of all of our outstanding common stock, excluding from the denominator shares of unvested restricted stock. If Shire and its affiliates beneficially own more than 19.9% of our outstanding common stock, we are obligated to redeem the shares of common stock in excess of such threshold at Shire's election at the then fair market value of the common stock. We are not obligated to redeem such excess shares to the extent that Shire may sell such excess shares of common stock without limitation pursuant to Rule 144 under the Securities Act.

Sanofi Collaboration and License Agreement

On June 8, 2018, our wholly owned subsidiary Translate Bio MA, Inc. entered into a collaboration and license agreement with Sanofi, which we refer to as the Sanofi Agreement, to develop mRNA vaccines for up to five infectious disease pathogens. The Sanofi Agreement became effective on July 9, 2018.

Under the Sanofi Agreement, we and Sanofi have agreed to collaborate to perform certain research and development activities to advance mRNA vaccines and mRNA vaccine platform development during a three-year research term, which may be extended by mutual agreement. The collaboration activities will be subject to a collaboration plan to be updated annually. The Sanofi Agreement provides for Sanofi to make an upfront payment to us of $45.0 million, which we received in July 2018, as well as certain potential milestone payments and option payments, each as further described below. In addition, we are eligible to receive from Sanofi tiered royalty payments on worldwide net sales of mRNA vaccines.

Under the Sanofi Agreement, we and Sanofi have created a governance structure, including committees and working groups, to manage the activities under the collaboration. If we and Sanofi do not mutually agree on certain decisions, Sanofi would be able to

break a deadlock without our consent. The collaboration plan includes an estimated budget. Sanofi is responsible for paying our employee costs, out-of-pocket costs paid to third parties and manufacturing costs, up to a specified amount.

Under the terms of the Sanofi Agreement, we have granted to Sanofi exclusive, worldwide licenses under applicable patents, patent applications, know-how and materials, including those arising under the collaboration, to develop, commercialize and manufacture mRNA vaccines to prevent, treat or cure diseases, disorders or conditions in humans caused by any of three infectious disease pathogens, which we call the Licensed Fields. In addition, pursuant to the terms of the Sanofi Agreement and subject to certain limitations, Sanofi has options to add up to two additional infectious disease pathogens within the granted licenses to the Licensed Fields by exercising either option or both options during a specified option term and paying us a $5.0 million fee per added pathogen. If, prior to the exercise of the options by Sanofi, we receive a bona fide third-party offer to acquire rights to the field to which an option relates, we must notify Sanofi of such offer, and if Sanofi does not exercise its option as to the applicable field, such field will no longer be subject to the option.

We and Sanofi retain the rights to perform our respective obligations and exercise our respective rights under the Sanofi Agreement, and Sanofi may grant sublicenses to affiliates or third parties. Sanofi has also granted us non-exclusive, sublicenseable licenses under patent rights claiming certain improvements that Sanofi may make to the technology we have licensed to it or claiming certain technology arising from the collaboration and owned by Sanofi. We may exercise such licenses to develop, manufacture and commercialize products, other than products that use a vaccine to prevent, treat or cure a disease, disorder or condition in humans caused by an infectious disease pathogen. If we commercialize any product covered by such a Sanofi patent right, we would pay Sanofi a royalty of a low single-digit percentage. Sanofi may terminate these licenses to us if we materially breach the terms of the license and the breach remains uncured for a specified period, which may be extended in certain circumstances.

Sanofi has sole responsibility for all commercialization activities for mRNA vaccines in the Licensed Fields and is obligated to bear all costs in connection with any such commercialization. We and Sanofi intend to enter into a supply agreement pursuant to which we would be responsible for manufacturing certain non-clinical and clinical mRNA vaccines and materials containing mRNA until we transfer such manufacturing capabilities to Sanofi. We would be entitled to receive payments for manufacturing mRNA vaccines under the supply agreement.

The Sanofi Agreement provides that we are eligible to receive aggregate potential payments of up to $805.0 million from Sanofi, which includes an upfront payment, potential milestone payments and potential option exercise payments. In July 2018, Sanofi paid us a $45.0 million upfront payment in respect of the licenses and options granted to Sanofi. Sanofi will also pay us $5.0 million with respect to each additional Licensed Field for which it exercises an option. Sanofi has also agreed to pay us milestone payments upon the achievement of specified development, regulatory and commercialization milestones. In particular, we are entitled to receive development and regulatory milestone payments of up to $63.0 million per Licensed Field and sales milestone payments of up to $85.0 million per Licensed Field. In addition, we are entitled to receive a $10.0 million milestone payment from Sanofi following completion of the technology and process transfer.

Sanofi has agreed to pay us a tiered royalty on worldwide net sales of all mRNA vaccines within each Licensed Field ranging from a high single-digit percentage to a low teens percentage, depending on quarterly net sales by Sanofi, its affiliates and its sublicensees. The royalty paid to us can be reduced with respect to a product once the relevant licensed patent rights expire or if additional licensed technology is required, but the royalty payments generally may not fall below our royalty obligations to third parties plus a royalty of a low single-digit percentage. Royalty payments under the Sanofi Agreement are payable on a product-by-product and country-by-country basis beginning on the launch of the product in the country until the later of the expiration of the last valid claim covering such product or 10 years after the launch of such product in such country.

The Sanofi Agreement provides that it will remain in effect until terminated in accordance with its terms. Either we or Sanofi may terminate the Sanofi Agreement in its entirety if the other party is subject to certain insolvency proceedings. Either party may terminate the Sanofi Agreement in its entirety or with respect to a particular Licensed Field, country or product if the other party materially breaches the Sanofi Agreement and the breach remains uncured for a specified period, which may be extended in certain circumstances. Sanofi may also terminate the Sanofi agreement in its entirety or with respect to a particular Licensed Field, country or product for safety reasons or for convenience, in each case after a specified notice period. After termination of the Sanofi Agreement, Sanofi may continue to manufacture and commercialize the terminated products for a specified period of time, subject to Sanofi's payment obligations.

License Agreements

Exclusive Patent License Agreement with MIT

In November 2013, Shire AG entered into an agreement with the Massachusetts Institute of Technology, or MIT, for a worldwide license, under specified patent rights owned by MIT, and Shire made a one-time, upfront payment of $75,000, plus

reimbursed certain patent expenses of MIT. In July 2015, Shire AG's successor Shire International GmbH and MIT amended the license agreement to include certain additional patent rights owned jointly by MIT and Shire related to inventions developed pursuant to a research agreement between MIT and Shire, and Shire made a one-time, upfront payment of $15,000. We acquired the license in December 2016 as part of our acquisition of the MRT Program from Shire. We and MIT amended the agreement on April 11, 2017 to modify the development milestone timetable discussed below.

The agreement grants us an exclusive license under the licensed patent rights to develop, manufacture and commercialize any product containing both (i) any RNA sequences, including mRNA, that encode a protein or peptide suitable for human therapeutic use, which may include operably linked non-coding sequences that facilitate translation of the coding portion of such RNA sequence, but such non-coding sequences do not include nucleic acids that function through an RNA interface mechanism or transcriptional activation mechanism, which RNA sequences we call the coding RNA component, and (ii) products covered by the licensed patent rights, which we call the lipid products. We call a product containing both a coding RNA component and a lipid product a licensed product. Under the licensed patent rights, we are permitted to develop, manufacture and commercialize the licensed products for the delivery of coding RNA components to treat disease in humans. The license is subject to certain rights retained by MIT and other non-profit research institutions for research, teaching and educational purposes, rights retained under law by the federal government due to its funding the creation of the invention and rights granted to the sponsor of the research resulting in the inventions permitting internal research by the sponsor and its research collaborators.

We have the right to grant sublicenses under this license. The patent rights licensed to us by MIT include claims that cover our customized LNPs used for delivery of coding RNA components in our MRT platform, including MRT5201 and products that may be developed under our collaboration with Sanofi.

Under the license agreement, we are obligated to make an annual license maintenance fee payment to MIT, payable on January 1 of each calendar year, of up to $0.2 million, which may be credited against royalties subsequently due on net sales of licensed products earned in the same calendar year. For each of the calendar years 2017 and 2018, we made annual license maintenance fee payments of $0.1 million to MIT.

We are also obligated to make milestone payments to MIT aggregating up to $1.375 million upon the achievement of specified clinical and regulatory milestones with respect to each licensed product and $1.250 million upon our first commercial sale of each licensed product, and to pay royalties of a low single-digit percentage to MIT based on our, and any of our affiliates' and sublicensees', net sales of licensed products. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances. Our obligation to make royalty payments extends with respect to a licensed product in a country until the expiration of the last-to-expire patent or patent application licensed from MIT covering the licensed product in the country. In addition, we are obligated to pay MIT a low double-digit percentage of the portion of income from sublicensees that we ascribe to the MIT-licensed patents, excluding royalties on net sales and research support payments. In 2019, pursuant to such provision, we have agreed to pay $0.7 million to MIT as their share of sublicense income with respect to the upfront payment received under the Sanofi Agreement as well as future option and milestone payments that we may receive pursuant to the Sanofi Agreement. The amounts that we may owe to MIT will depend upon the relative value of the patents we licensed from MIT and sublicensed to Sanofi as compared to the other rights that we licensed to Sanofi. The determination of the relative value of such rights is subject to a process described in our license agreement with MIT.

The agreement obligates us to use commercially reasonable efforts and expend a minimum amount of resources each year to develop licensed products in accordance with a development plan and a development milestone timetable specified in the agreement, to use commercially reasonable efforts to commercialize licensed products and, upon commercialization, to make the licensed products reasonably available to the public.

MIT has the right to terminate the agreement if we fail to pay amounts when due or otherwise materially breach the agreement and fail to cure such nonpayment or breach within specified cure periods or in the event we cease to carry on our business related to the agreement. In the event of a termination due to our breach caused by a due diligence failure of a licensed product, but where we have fulfilled our obligations with respect to a different licensed product, MIT may not terminate the agreement with respect to the different licensed product. MIT may immediately terminate the agreement if we or any of our affiliates bring specified patent challenges against MIT or assist others in bringing a patent challenge against MIT. We have the right to terminate the agreement for our convenience at any time on three months' prior written notice to MIT and payment of all amounts due to MIT through the date of termination.

Our patent rights, and the rights of our affiliates and sublicensees, in specified licensed products may also terminate, if, after November 1, 2018, we, our affiliates or MIT receive a request from a third party to develop such licensed product for which we are unable to, within nine months of receiving notice of any such request, either demonstrate that we have initiated a fully funded project for the commercial development of such licensed product and provide a business plan with acceptable milestones; demonstrate that the

licensed product proposed by such third party would be competitive with a licensed product for which we have initiated a fully funded project; or enter into a sublicense agreement with such third party on commercially reasonable terms, and, in each case, MIT, in its sole discretion, grants a license to such third party for the specified patent rights. As of March 14, 2019, we have not received any such request.

Agreement with Ethris GMBH

In December 2012, Shire AG entered into a research collaboration and license agreement with Ethris GMBH, or Ethris. While the research collaboration and license agreement has ended, certain rights survive its termination. With respect to patents and patent applications arising out of the agreement that pertain to the MRT5005 product that are jointly owned by Ethris and us, we and Ethris each have the right to practice and to exploit the jointly owned intellectual property without the approval of the other party. These rights include the right to license or assign the technology of the jointly owned intellectual property to a third party without the approval of the other party.

Intellectual Property

Our commercial success depends in part on our ability to obtain, maintain and enforce our proprietary and intellectual property rights relating to our programs and our core technologies for messenger RNA therapeutics, including discoveries, developments in improvements of mRNA compositions, manufacturing techniques and analytics, as well as lipid nanoparticle and other delivery vehicle compositions, manufacturing techniques and analytics. Our success also depends in part on our ability to develop and commercialize therapeutic products without infringing on the proprietary rights of others. Our policy is to seek to protect our proprietary and intellectual property positions by, among other methods, filing U.S. and foreign patent applications relating to technology important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing innovation to develop, maintain and expand our proprietary and intellectual property positions.

We file patent applications directed to our key programs, including MRT5005 and MRT5201, in an effort to establish broad and dominant intellectual property positions regarding new compositions relating to these programs as well as uses of these and similar compositions in the treatment of relevant diseases. We also seek patent protection with respect to methods of making these compositions and to therapeutic biomarkers that may be useful in establishing or monitoring the efficacy of these compositions in patients. As of December 31, 2018, we owned or licensed 38 issued or allowed U.S. patents, 51 U.S. pending non-provisional patent applications, 60 issued or allowed foreign patents, 175 foreign pending patent applications, and 41 pending Patent Cooperation Treaty, or PCT, or provisional patent applications relating to mRNA therapeutics. The foreign issued patent and patent applications are in a number of jurisdictions, including Europe, including Eastern Europe, North America including Canada and Mexico, Australia, Asia, India and South America.

The intellectual property portfolios for our most advanced programs as of December 31, 2018, are summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO can be significantly narrowed by the time they issue, if they issue at all. We expect this could be the case with respect to some of our pending patent applications referred to below.

MRT5005

The intellectual property portfolio for our MRT5005 program includes patents and applications directed to compositions for the mRNA component of MRT5005 as well as analogs thereof, to compositions for the delivery vehicle component of MRT5005 as well as analogs thereof, to compositions for the combination of the mRNA delivery vehicle components of MRT5005, as well as to methods for using and making these novel compositions. As of December 31, 2018, we owned or licensed nine issued or allowed U.S. patents, six issued or allowed European patents, 13 pending non-provisional U.S. patent applications, seven pending European patent applications, at least 46 other foreign patents and patent applications in a number of jurisdictions, and six pending PCT or provisional patent applications relating to our MRT5005 program. The U.S. or ex-U.S. issued patents or patents issuing from these pending applications for our MRT5005 program will have a statutory expiration date from 2030 to 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

MRT5201

The intellectual property portfolio for our MRT5201 program includes patents and patent applications directed to compositions for the mRNA component of MRT5201 as well as analogs thereof, to compositions for the delivery vehicle component of MRT5201 as well as analogs thereof, to compositions for the combination of the mRNA and delivery vehicle components of MRT5201, as well as to methods for using and making these novel compositions. As of December 31, 2018, we owned or licensed 12 issued or allowed

U.S. patents, four issued or allowed European patents, 13 pending U.S. patent applications, nine pending European patent applications, at least 67 other foreign patents and patent applications in a number of jurisdictions, and five pending PCT or provisional patent applications relating to our MRT5201 program. The U.S. or ex-U.S. issued patents or patents issuing from the pending applications covering our MRT5201 program will have a statutory expiration date from 2030 to 2038. Patent term adjustments or patent term extensions could result in later expiration dates.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each medicine and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property positions for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, it may happen that certain patent applications that we have filed or may file, or that we have licensed or may license from third parties, may not result in the issuance of corresponding patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, we may have to participate in proceedings in the USPTO to determine invention rights, which could result in substantial costs to us, even if the eventual outcome is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may remain in force for a short period following commercialization, thereby reducing any advantage of any such patent.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with any future collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us ownership of technologies that are developed through a relationship with a third party.

With respect to our proprietary mRNA therapeutic technology platform, we consider trade secrets and know-how to be an important component of our intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to this technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

Sales and Marketing

In light of our stage of development, we have not yet established a commercial organization or distribution capabilities. We have retained worldwide commercial rights for our product candidates. If our product candidates receive marketing approval, we plan to commercialize them in the United States and potentially in Europe with our own focused, specialty sales force. We would expect to conduct most of the buildout of this organization following approval in the United States or similar marketing authorization in Europe of any of our product candidates. We expect to explore commercialization of MRT5005 and potentially other product candidates in certain markets outside the United States, including the European Union, utilizing a variety of collaboration, distribution and other marketing arrangements with one or more third parties.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated clinical-trial scale demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

Government Regulation and Product Licensure

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, sales, reimbursements, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our mRNA-based therapies would be licensed by the FDA as biological products, or biologics, under the Public Health Service Act, or PHSA, and regulated under the Federal Food, Drug and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical trials, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines and civil or criminal investigations and penalties brought by the FDA or Department of Justice, or DOJ, or other government entities, including state agencies.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps before the product candidate will be licensed by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, purity and efficacy of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of a biologics license application, or BLA, for a biologic product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the BLA;

- payment of user fees and securing FDA licensure of the BLA to allow marketing of the new biologic product; and

- compliance with any post-approval requirements, including the potential requirement to implement a REMS and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Clinical holds are typically imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution 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 continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about specified clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational products for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients.

During Phase 1 clinical trials, information about the investigational biological product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic: such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, 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 are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product 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. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Safety and Innovation Act. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits a BLA three years after the date of enactment of that statute must submit pediatric assessments with the BLA if the biologic is intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Review and Approval of a BLA

In order to obtain approval to market a biological product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity, potency and efficacy of the proposed biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the biological product to the satisfaction of the FDA.

The BLA is, thus, a vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new biologic product candidate must be the subject of an approved BLA before it may be commercialized in the United States. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2019 is approximately $2.6 million for an application requiring clinical data. The sponsor of an approved BLA is also subject to a program fee for fiscal year 2019 of approximately $0.3 million. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of a BLA, the FDA conducts a preliminary review of the application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within 10 months from the date on which the FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of products that are not NMEs, the 10-month and 6-month review periods run from the date that the FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with a BLA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application 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. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. 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 under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited 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 are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the

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. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement 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 product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority 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 10 months to 6 months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the 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 condition 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 irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products 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 where 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 clinical benefit of a product.

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 product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products 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 trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

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 product'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 confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on a BLA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a new product, it may limit the approved indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess 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 holds on post-approval clinical trials;

- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or

- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits 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.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a biologic product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting a BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product

for different conditions. If a biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same biologic for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2019, the FDA has approved 17 biosimilar products for use in the United States. No interchangeable biosimilars, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by the FDA in the near term.

Under the Act, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of biologic products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing 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;

- the federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or 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, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, 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, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as 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, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. 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.

Pharmaceutical Insurance Coverage

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. 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 are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost-effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Health Care Reform

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- 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;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and

- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2025 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Further, since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session. Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the Administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued such payments were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. Congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. Congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the

relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump Administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

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. In addition, regional health care 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 additional state and federal 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 reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union, or EU, generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU. We anticipate that our mRNA-based therapies designed to treat diseases caused by protein or gene dysfunction will be regulated as advanced therapy medicinal products, or ATMPs, in the EU. Additionally, there may be local legislation in various EU Member States, which may be more restrictive than the EU legislation, and we would need to comply with such legislation to the extent it applies.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of ATMPs. The sponsor must take out a clinical trial insurance policy and, in most EU countries, the sponsor is liable to provide "no fault" compensation to any study subject injured in the clinical trial.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation was published on June 16, 2014 but is not expected to apply until later in 2019. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU 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 EU 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.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. 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 (CHMP) or Committee for Advanced Therapies (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.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (that is, the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, ATMPs and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

The CAT is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a marketing authorization application is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that it is likely that our compliance with them will be necessary to gain and maintain approval for any of our product candidates.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances." Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;

- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and

- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) 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 and/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.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the

national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the Concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the European Union

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 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. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. 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 EU 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. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the 10-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the EU will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty, being March 29, 2019. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the EU. If no formal withdrawal agreement is reached between the United Kingdom and the EU, then it is expected the United Kingdom's membership in the EU will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the EU. Discussions between the United Kingdom and the EU focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the EU on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements

relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also 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. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. 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 trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. 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 products, if approved in those countries.

Employees

As of December 31, 2018, we had 81 full-time employees, including a total of 25 employees with M.D., Pharm.D. or Ph.D. degrees. Of these full-time employees, 55 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Reorganization

We are a Delaware corporation that was incorporated on November 10, 2016 under the name RaNA Therapeutics, Inc. On December 5, 2016, we completed a series of transactions, which we refer to as the "Reorganization," pursuant to which RaNA Therapeutics, LLC, or RaNA LLC, became a direct, wholly owned subsidiary of RaNA Therapeutics, Inc., and all of the outstanding equity securities of RaNA LLC were exchanged for equity securities of RaNA Therapeutics, Inc. The purpose of the Reorganization was to reorganize our corporate structure so that our existing investors would own capital stock in a corporation rather than equity interests in a limited liability company. On June 26, 2017, we changed our name from RaNA Therapeutics, Inc. to Translate Bio, Inc. On December 19, 2017, RaNA LLC merged with and into Translate Bio, Inc., with Translate Bio, Inc. continuing as the surviving corporation.

Corporate Information

Our principal executive offices are located at 29 Hartwell Avenue, Lexington, Massachusetts 02421, and our telephone number is (617) 945-7361.

Information Available on the Internet

Our internet website address is www.translate.bio. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities and Exchange Act of 1934, as amended, or the Exchange Act. We make these reports available through the "Financials and Flings" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at *http://www.sec.gov*.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this Annual Report on Form 10-K, including our financial statements and the related notes and in our other filings with the Securities and Exchange Commission, or SEC. If any of the following risks occur, our business, financial condition, results of operations and prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant losses. Our net losses were $97.4 million and $66.4 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $246.2 million. As noted below, we and our auditors have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. We have funded our operations to date primarily with proceeds from the sale of redeemable convertible preferred stock and the sale of bridge units, which ultimately converted into shares of our preferred stock, the proceeds from our IPO and an upfront payment received under the Sanofi Agreement. We expect that it could be several years, if ever, before we have a commercialized product candidate. We expect to continue to incur significant expenses and operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

- continue the clinical development of MRT5005 and pursue the clinical development of MRT5201;
- leverage our programs to advance our other product candidates into preclinical and clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- seek to discover and develop additional product candidates;
- establish a sales force, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- hire additional clinical, quality control and scientific personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- maintain, expand and protect our intellectual property portfolio;

- acquire or in-license other product candidates and technologies; and
- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we, or our collaborators, must develop and eventually commercialize product candidates with significant market potential. This will require us to succeed in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate sufficient revenue to achieve profitability. 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 the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

We have never generated revenue from product sales and may never be profitable.

We have never generated revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with our collaborative partners, to successfully develop and obtain the regulatory approvals necessary to commercialize our product candidates. We do not have any products approved for sale and do not anticipate generating revenue from product sales for the next several years, if ever. Our ability to generate future revenue from product sales depends heavily on our, or our collaborators', success in:

- completing preclinical and clinical development of our product candidates and identifying and developing new product candidates;
- seeking and obtaining marketing approvals for any of our product candidates;
- launching and commercializing product candidates for which we obtain marketing approval by establishing a sales force, marketing, medical affairs and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- achieving formulary status in hospitals and adequate coverage and reimbursement by government and third-party payors for our product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- defending against third-party interference or infringement claims, if any; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs in commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory agencies to perform clinical trials or studies in addition to those that we currently anticipate. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

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

Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights, conducting discovery, research and development activities for our programs, undertaking preclinical studies, entering into licensing agreements and planning for potential commercialization. While we are conducting a Phase 1/2 clinical trial of MRT5005 and filed an investigational new drug application, or IND, for MRT5201, which the FDA has placed on clinical hold while we conduct additional preclinical studies, we have not yet completed a clinical trial of any of our product candidates. We have not yet demonstrated the ability to obtain marketing approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any evaluation of our business to date or predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

If we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, reduce or eliminate certain of our product development efforts or other operations.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of and seek marketing approval for our product candidates. These expenditures will include costs associated with our asset purchase agreement, as amended, with Shire Human Genetic Therapies, Inc., or Shire, a subsidiary of Shire plc, or the Shire Agreement. Under the terms of the Shire Agreement, we are obligated to make significant cash payments upon the achievement of specified commercial milestones, as well as earnout payments in connection with sales of products based on the compounds that we acquired from Shire.

We will require additional capital to advance MRT5005 and MRT5201 and any other product candidates we develop through necessary clinical trials and clinical development. In addition, if we obtain marketing approval for any of our product candidates that we plan to commercialize ourselves, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain additional funding in connection with our continuing operations. We may raise this additional funding through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions and funding under government or other contracts. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

We believe that our existing cash, cash equivalents and short-term investments of $144.1 million as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. As of December 31, 2018, management has further assessed this risk and, in accordance with the requirements of Accounting Standards Update No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, or ASC 205-40, determined that there is substantial doubt about our ability to continue as a going concern. There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations. If we are unable to obtain funding, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could adversely affect our business prospects, and we may be unable to continue operations. To finance our operations beyond that point, we will need to raise additional capital, which cannot be assured.

Furthermore, our future funding requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;

- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the success of our collaboration with Sanofi;
- the ability to receive additional non-dilutive funding, including grants from organizations and foundations;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the cost and timing of hiring new employees to support our continued growth;
- costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies;
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any; and
- our ability to continue as a going concern.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that typically takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenue, if any, and any commercial milestones or royalty payments under any collaboration agreements that we enter into, including our collaboration with Sanofi, will be derived from or based on sales of products that may not be commercially available for many years, if at all. Accordingly, we will continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline, and our stockholders may not agree with our financing plans or the terms of such financings.

Our failure to raise capital as and when needed would negatively impact our financial condition and our ability to pursue our business strategy, and we could be forced to delay, reduce or eliminate certain of our research and development programs or any future commercialization efforts.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through the combination of public or private equity offerings, debt financings, grants, collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring debt, making capital expenditures or declaring dividends. In addition, debt financing would result in increased fixed payment obligations.

If we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we will be required to delay, reduce or eliminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

As of December 31, 2018, we had $144.1 million in existing cash, cash equivalents and short-term investments. We expect these available cash resources to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. The report from our independent registered public accounting firm for the year ended December 31, 2018 includes an explanatory paragraph stating that our recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, we may be forced to delay or reduce the scope of our development programs, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. Future reports from our independent registered public accounting firm may also contain statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide funding to us on commercially reasonable terms, if at all.

We may be required to make payments in connection with our acquisition of the MRT Program from Shire.

In December 2016, we acquired the messenger RNA, or mRNA, therapeutic platform, or MRT Program, pursuant to the Shire Agreement. Under the Shire Agreement, we are obligated to make milestone payments to Shire of up to $60.0 million in the aggregate upon the occurrence of specified commercial milestones, including upon the first commercial sale of a product that includes or is composed of MRT compounds acquired from Shire, or MRT Product, for the treatment of cystic fibrosis, or CF, and upon the achievement of a specified level of annual net sales with respect to MRT Products. We are also obligated to make additional milestone payments of $10.0 million for each non-CF MRT Product upon the first commercial sale of a non-CF MRT Product; provided that such milestone payments will only be due once for any two non-CF MRT Products that contain the same MRT compounds or once per non-CF MRT Product that is a vaccine developed under our collaboration with Sanofi. Under the Shire Agreement, we are also obligated to pay a fixed, quarterly earnout payment of a mid-single-digit percentage of net sales of each MRT Product. The earnout period will begin on the date of the first commercial sale of MRT Products and will end, on a product-by-product and country-by-country basis, on the later of (1) the expiration of the last valid claim of the assigned patents covering the manufacture, use or composition of such product in such country of the applicable MRT Product and (2) 10 years after the first commercial sale of the MRT Product in such country. If these payments become due under the terms of the Shire Agreement, we may not have sufficient funds available to meet our obligations and our development efforts may be materially harmed. If a combination MRT Product that is a vaccine is sold, in certain circumstances, we would be obligated to pay Shire a royalty on a minimum portion of net sales.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the Tax Act, which significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The Tax Act contains, among other things, significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the Tax Act. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge prospective investors in our common stock to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2018, we had federal net operating loss carryforwards of $190.8 million, of which $122.1 million will, if not utilized, begin to expire in 2031. As of December 31, 2018, we had state net operating loss carryforwards of $171.7 million, which will, if not utilized, begin to expire in 2031. Our federal and state research and development tax credit carryforwards of $5.1 million and $2.0 million, respectively, will, if not utilized, begin to expire in 2032 and 2028, respectively, and orphan drug tax credit carryforwards of $6.6 million will, if not utilized, begin to expire in 2037. We also have state investment tax credit carryforwards of $0.4 million, which will, if not utilized, begin to expire in 2019. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset our future income tax liabilities. Under federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80% of our taxable income in the year in which such carryforwards are used.

In addition, under Section 382 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards are subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

Risks Related to the Development of Our Product Candidates

Our approach to the discovery and development of product candidates based on mRNA is unproven, and we do not know whether we will be able to successfully develop any products.

We focus on delivering mRNA encoding functional versions of proteins into cells without altering the underlying DNA. Our future success depends on the successful development of this novel therapeutic approach. Relatively few mRNA-based therapeutic product candidates have been tested in animals or humans, and the data underlying the feasibility of developing mRNA-based therapeutic products is both preliminary and limited. To date, no product that utilizes mRNA as a therapeutic has been approved in the United States or Europe. We have not yet succeeded and may not succeed in demonstrating the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. We have not yet completed a clinical trial of any product candidate and we have not yet assessed safety of any product candidate in humans. As such, there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our MRT platform, or any similar or competitive mRNA platforms, will result in the development and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our MRT platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

We have never obtained marketing approval for a product candidate, and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We are a clinical-stage company and have not received approval from the FDA, EMA or other regulatory authority to market any product candidate. The regulatory review process may be more expensive or take longer than we expect, and we may be required to conduct additional studies and/or trials beyond those we anticipate. If it takes us longer to develop and/or obtain regulatory approval for our product candidates than we expect, such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

The FDA placed the IND for our planned Phase 1/2 clinical trial of MRT5201 on clinical hold, requiring us to submit additional information before we may be permitted to initiate the trial, and if the clinical hold is not lifted, we will not be able to initiate our clinical trial of MRT5201.

In December 2018, we submitted to the FDA an IND to initiate a Phase 1/2 clinical trial of MRT5201. This trial is not yet active at any investigational site and has not yet recruited any subjects. Prior to initiating the trial, we will be required to resolve a clinical hold on the IND outlined in a February 2019 letter to us from the FDA. In its correspondence, the FDA requests additional preclinical toxicology data to assess the potential for adverse effects related to the clearance time of MRT5201. We have identified the additional

preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019, after which the FDA will have 30 days to respond. If the clinical hold is not lifted, or if there is a delay in lifting the clinical hold, we may not be able to initiate our clinical trial of MRT5201 in 2019, or at all. Any delay in our ability, or our inability, to initiate our clinical trial of MRT5201 because of the clinical hold will delay or terminate our clinical development plans for MRT5201, may require us to incur additional clinical development costs and could impair our ability to ultimately obtain FDA approval for MRT5201. Delays in the completion of any clinical trial of MRT5201 could increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue.

In the near term, we are dependent on the success of MRT5005 and MRT5201. If we are unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize MRT5005 and MRT5201, either alone or with a future collaborator, or if we experience significant delays in doing so, our business would be substantially harmed.

We do not currently have products approved for sale and are investing a significant portion of our efforts and financial resources in the development of MRT5005 and MRT5201. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop and obtain marketing approval for, and successfully commercialize, MRT5005 and MRT5201 in one or more disease indications.

The success of MRT5005 and MRT5201 will depend on several factors, including the following:

- successful initiation of clinical trials, including a lift by the FDA of the clinical hold on the IND for our planned clinical trial of MRT5201;
- successful patient enrollment in and completion of clinical trials;
- a safety, tolerability and efficacy profile that is satisfactory to the FDA, EMA or other regulatory authorities for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment and maintenance of arrangements with third-party manufacturers for both clinical and any future commercial manufacturing;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by hospitals, the patient community, the medical community and third-party payors;
- the availability of coverage and adequate reimbursement from third-party payors;
- the performance of our future collaborators, if any; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical development, whether or not the FDA lifts the clinical hold on the IND for our planned clinical trial of MRT5201, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize MRT5005 and MRT5201, on our own or with any future collaborator, or experience delays as a result of any of these factors or otherwise, our business would be substantially harmed.

Clinical drug development is a lengthy and expensive process with uncertain timelines and uncertain outcomes. If the initiation or completion of clinical trials of our product candidates, particularly MRT5005 and MRT5201, is prolonged or delayed, we or any future collaborators may be unable to obtain required regulatory approvals, and therefore will be unable to commercialize our product candidates on a timely basis or at all, which will adversely affect our business.

Before obtaining marketing approval for our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive, time-consuming, difficult to design and implement and uncertain as to outcome. We cannot guarantee that our clinical trials, such as our Phase 1/2 clinical trial of MRT5005 in patients with CF, will be conducted as planned, completed on schedule, if at all, or yield positive results.

A clinical trial failure can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory authorities or collaborators on trial design;
- delays in successfully addressing the specific information requests made by the FDA with respect to the clinical hold placed on the IND for our planned Phase 1/2 clinical trial of MRT5201;
- delays in reaching agreement on acceptable terms with contract research organizations, or CROs, and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board or independent ethics committee approval at each clinical trial site;
- delays in recruiting suitable subjects or a sufficient number of subjects to participate in our clinical trials;
- imposition of a clinical hold by regulatory authorities, including upon submission of an IND, such as the clinical hold that the FDA has placed on the IND for our planned Phase 1/2 clinical trial of MRT5201 in January 2019 and the clinical hold that the FDA had placed on the IND for our Phase 1/2 clinical trial of MRT5005 in January 2018 and subsequently lifted in April 2018, or as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- failure by us, any CROs we engage, clinical investigators or any other third parties to adhere to clinical trial requirements;
- failure to perform the clinical trial in accordance with good clinical practices, or GCP, or applicable regulatory requirements in the European Union, the United States, or other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- delays or failures in demonstrating the comparability of product manufactured at one facility or with one process to product manufactured at another facility or with another process, including clinical trials to demonstrate such comparability;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or subjects dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; and
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional trials to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

We could encounter delays if a clinical trial is suspended or terminated by us, by the institutional review boards of the institutions in which such trials are conducted or their ethics committees, by the Data Review Committee or Data Safety Monitoring Board for such trial or by the FDA or other foreign regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, including those relating to the class of products to which our product candidates belong.

Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates or early termination of the development of our product candidates.

Preclinical drug development is uncertain. Some or all of our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these product candidates on a timely basis or at all, which would have an adverse effect on our business.

In order to obtain FDA approval to market a new biological product, we must demonstrate proof of safety, purity and potency or efficacy in humans. To satisfy these requirements, we will have to conduct adequate and well-controlled clinical trials. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned IND in the United States. We cannot be certain of the timely completion or outcome of our preclinical testing and studies, and we cannot predict if the FDA will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of these product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for any preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. For example, in December 2018, we submitted an IND to the FDA supporting the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Subsequently, the FDA notified us that our IND for MRT5201 was placed on clinical hold. While we are conducting additional preclinical studies required in support of our IND, we cannot be certain that the data obtained and submitted to the FDA will be accepted and that our clinical trial for MRT5201 will be allowed to begin. In addition, after we submitted an IND for MRT5005 to initiate our Phase 1/2 clinical trial in patients with CF, the FDA placed a clinical hold on the IND, requiring us to submit, prior to initiating the trial, additional chemistry, manufacturing and controls information relating to materials and processes used during the manufacture of the product candidate. The FDA lifted the clinical hold for our Phase 1/2 clinical trial of MRT5005 in April 2018.

Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity, novelty and intended use of the product candidate, and often can be several years or more per product candidate. Delays associated with product candidates for which we are conducting preclinical testing and studies ourselves may cause us to incur additional operating expenses. Moreover, we may be affected by delays associated with the preclinical testing and studies of certain product candidates conducted by our potential partners over which we have no control. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical trials; and
- delays in reaching a consensus with regulatory agencies on study design.

Moreover, even if we do initiate clinical trials for other product candidates, our development efforts may not be successful, and clinical trials that we conduct or that third parties conduct on our behalf may not demonstrate sufficient safety, purity and potency or efficacy necessary to obtain the requisite regulatory approvals for any of our product candidates or product candidates employing our technology. Even if we obtain positive results from preclinical studies or initial clinical trials, we may not achieve the same success in future trials.

Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.

Results from preclinical studies are not necessarily predictive of clinical trial results, results from early clinical trials are not necessarily predictive of later clinical trial results and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or successful advancement through initial clinical trials.

There can be no assurance that the success we achieved in preclinical studies of MRT5005 or MRT5201 or may achieve in preclinical studies of other product candidates will result in success in clinical trials of these product candidates. In addition, we cannot assure you that we will be able to achieve the same or similar success in our preclinical studies and clinical trials of our other product candidates.

Our preclinical studies in animal models have been conducted using human mRNA, which differs from animal mRNA, making it difficult for us to use animal models to assess whether our product candidates are safe or effective in humans. In particular, the preclinical studies we have conducted in rats and non-human primates are not indicative of clinical trial outcomes in CF, as success of treatment of CF in animals does not predict success in humans.

We have not completed any clinical trials evaluating any of our product candidates or proposed delivery modes, including the use of lipid-based nanoparticles, or LNPs, that are customized for delivery to specific tissues.

There is a high failure rate for drugs and biologic products proceeding through preclinical studies and clinical trials. Any product candidates we develop may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical studies and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

We may find it difficult to enroll and dose patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying, qualifying and enrolling patients to participate in clinical trials of our product candidates is critical to our success, and we may not be able to identify, recruit, enroll and dose a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. The timing of our clinical trials depends on our ability to recruit patients to participate as well as to subsequently dose these patients and complete required follow-up periods. In particular, because our clinical trial of MRT5005 and our planned clinical trial of MRT5201 are focused on indications with relatively small patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. Many CF clinical trial sites place importance on the review, ranking and sanctioning of CF patient advocacy groups. If CF patient advocacy groups do not timely sanction or highly rate our clinical trials, or prioritize trials of other sponsors over our trials, we may not be able to enroll sufficient patients to conduct our trials at their member sites, or it may take longer to conduct these trials.

In addition, we may experience enrollment delays related to increased or unforeseen regulatory, legal and logistical requirements at certain clinical trial sites. These delays could be caused by regulatory reviews by regulatory authorities and contractual discussions with individual clinical trial sites. Any delays in enrolling and/or dosing patients in our planned clinical trials could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in our competitors' clinical trials. Patient enrollment may also be affected by other factors, including:

- coordination between us, CROs and any future collaborators in our efforts to enroll and administer the clinical trial;
- size of the patient population and process for identifying patients;

- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- availability of competing commercially available therapies and other competing product candidates' clinical trials;
- time of year in which the trial is initiated or conducted;
- variations in the seasonal incidence of the target indication;
- severity of the disease under investigation;
- ability to obtain and maintain subject consent;
- ability to enroll and treat patients in a timely manner;
- risk that enrolled subjects will drop out before completion of the trial;
- proximity and availability of clinical trial sites for prospective patients;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing.

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates for which there is a greater likelihood of commercial success.

Our success depends upon our ability to identify, develop and commercialize product candidates based on our MRT platform. If we do not successfully develop and eventually commercialize products, we will not be able to generate product revenue, resulting in significant harm to our financial position and adverse effects to our share price. Research programs to identify new product candidates require substantial technical, financial and human resources. Although our product candidates are currently in preclinical or clinical development, we may fail to identify other potential product candidates for clinical development.

Additionally, because we have limited financial and managerial resources, we may forego or delay pursuit of opportunities for certain programs or product candidates or for indications that later prove to have greater commercial potential. For example, we currently intend to focus our capital resources primarily on the clinical development of MRT5005 and MRT5201. However, the development of MRT5005 and MRT5201 may ultimately prove to be unsuccessful or less successful than another product candidate in our pipeline that we might have chosen to pursue on a more aggressive basis with our capital resources. Our estimates regarding the potential market for our product candidates could be inaccurate, and our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaborative arrangement.

If any of these events occur, we may be forced to abandon or delay our development efforts with respect to a particular product candidate, or we may fail to develop a potentially successful product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may fail to demonstrate safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities.

If the results of any of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as contraindications or warnings, including a black box warning;
- be sued; or
- experience damage to our reputation.

If serious adverse or undesirable side effects are identified during the development of our product candidates or proposed delivery modes, we may abandon or limit our development of such product candidates.

If our product candidates or proposed delivery modes are associated with undesirable side effects or have unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects or raise other safety issues that delayed or prevented further development of the compound. Further, given the relatively small patient populations for which we are developing our product candidates, we expect to have to evaluate long-term exposure to establish the safety and tolerability of our product candidates in a chronic dose setting. The adverse effects from long-term exposure, as well as exposure in general, to our product candidates are unknown because they are a new class of therapeutics that have never been evaluated in a clinical trial. The risk of adverse or undesirable side effects therefore remains a significant concern, and we cannot assure you that these or other risks will not occur in any of our current or future clinical trials of MRT5005, MRT5201 or other product candidates that we may develop.

If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business, financial condition, results of operations and prospects.

Because we are developing product candidates for the treatment of diseases in which there is little clinical experience using new technologies, there is increased risk that the FDA, the EMA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop. Because our initial focus is to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, there is heightened risk that the FDA, the EMA or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA determines that our success criteria is sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance.

This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Further, even if we do achieve the pre-specified criteria, the results may be unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. The EMA and other regulatory authorities may make similar comments with respect to these endpoints and data. Any product candidate we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval.

We may conduct clinical trials at sites outside the United States. The FDA may not accept data from trials conducted in such locations, and the conduct of trials outside the United States could subject us to additional delays and expense.

We may conduct one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with GCP. The FDA must be able to validate the data from the trial through an onsite inspection, if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, whether the FDA accepts the data will depend upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of MRT5005, MRT5201 or any future product candidates.

In addition, conducting clinical trials outside the United States could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

The manufacture of mRNA-based therapeutics is complex and manufacturers often encounter difficulties in production. If we or any of our third-party manufacturers encounter difficulties, our ability to provide product candidates for clinical trials or products, if approved, to patients could be delayed or halted.

The manufacture of mRNA-based therapeutics is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. We and our third-party manufacturers must comply with current Good Manufacturing Practices, or cGMP, regulations and guidelines for the manufacturing of our product candidates used in preclinical studies and clinical trials and, if approved, marketed products. Manufacturers of biotechnology products often encounter difficulties in production, particularly in scaling up and validating initial production. Furthermore, if microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities where our product candidates are made, such manufacturing facilities may be closed for an extended period of time to investigate and remedy the contamination. Shortages of raw materials may also extend the period of time required to develop our product candidates.

We cannot assure you that any disruptions or other issues relating to the manufacture of any of our product candidates will not occur in the future. Any delay or interruption in the supply of clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse developments affecting clinical or commercial manufacturing of our product candidates or products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could delay or impede the development and commercialization of any of our product candidates or products and could have an adverse effect on our business, prospects, financial condition and results of operations.

If the market opportunities for our product candidates are smaller than we believe they are, even assuming approval of a product candidate, our business may suffer.

Our product candidates are based on novel therapeutic approaches. As such, physicians, hospitals, third-party payors and patients may not accept our product candidates as treatment options, even if approved. While we believe there are commercial opportunities for our product candidates, we cannot be sure that is the case, particularly given the novelty of mRNA-based therapeutics.

Our projections of both the number of people affected by disease within our target indications, as well as the subset of these people who could 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 and 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. Likewise, 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 reach, which would adversely affect our results of operations and our business.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use mRNA, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecules. The competition is likely to come from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

Our competitors also include companies that are or will be developing other mRNA technology methods as well as small molecules, biologics and nucleic acid-based therapies for the same indications that we are targeting with our mRNA-based therapeutics.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even greater concentration of resources among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products faster or earlier than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors' products. In addition, the availability of our competitors' products could limit the demand and the prices we are able to charge for any products that we may develop and commercialize.

If approved for the treatment of CF, MRT5005 would compete with Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor) and Symdeko (tezacaftor/ivacaftor and ivacaftor), each of which is marketed by Vertex Pharmaceuticals Incorporated, or Vertex. Vertex also has several CFTR corrector compounds in clinical development, including VX-659, VX-445, VX-440, VX-152, VX-371 and VX-561, each of which is currently in Phase 3 or Phase 2 clinical trials.

We are aware of several companies with product candidates for the treatment of CF in Phase 2 clinical development in addition to Vertex, including AbbVie Inc., Corbus Pharmaceuticals, Inc., Flatley Discovery Lab, LLC, Laurent Pharmaceuticals Inc., Novoteris LLC, Protalix BioTherapeutics, Inc., Proteostasis Therapeutics, Inc., Spyryx Biosciences, Inc. and Verona Pharma plc. We are aware of several companies with product candidates for the treatment of CF in Phase 1 clinical development, including AbbVie Inc., Alaxia SAS, AstraZeneca plc, Boehringer Ingelheim GmbH, Chiesi Farmaceutici S.p.A., Eloxx Pharmaceuticals Ltd, Flatley Discovery Lab, LLC, Ionis Pharmaceuticals, Inc., Paranta Biosciences Ltd., ProQR Therapeutics N.V. and Proteostasis Therapeutics, Inc.

Other companies developing products that modulate or affect CFTR function for the treatment of CF also include: CRISPR Therapeutics AG, Editas Medicine Inc., Moderna, Inc. and Oxford BioMedica plc.

There are currently no approved therapies that address the underlying cause of OTC deficiency. There are several ammonia scavengers that treat OTC deficiency, including Buphenyl and Ravicti, each marketed by Horizon Pharma plc, and Ammonul, marketed by Swedish Ophan Biovitrum AB and Bausch Health Companies Inc. We are aware of several product candidates in clinical development for the treatment of OTC deficiency that may compete with MRT5201. DTX is an adeno-associated virus, or AAV, OTC gene stimulator in Phase 2 clinical development by Ultragenyx Pharmaceutical Inc. Synlogic, Inc. has a candidate, SYNB1020, in a Phase 1b/2a clinical trial that may relate to the treatment of liver disease with hyperammonemia. HepaStem/Heparesc is a liver progenitor cell-based therapy in Phase 2 clinical development by Promethera Biosciences S.A. Lunar-OTC is an OTC gene stimulator in preclinical development by Arcturus Therapeutics Ltd. SEL-313 is an AAV-based gene therapy in preclinical development by Selecta Biosciences, Inc. in collaboration with Genetheon S.A.

Other companies developing products that modulate or affect OTC function for the treatment of OTC deficiency include Ultragenyx Pharmaceutical Inc., Selecta Biosciences, Inc., Arcturus Therapeutics Ltd. and Synlogic, Inc.

Risks Related to Dependence on Third Parties

We expect to depend on collaborations with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected.

As part of our strategy, we intend to seek to enter into collaborations with third parties for one or more of our programs or product candidates. For example, in June 2018, we entered into a collaboration and license agreement with Sanofi to develop mRNA vaccines for up to five infectious disease pathogens. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that any future collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them.

Any collaborations we enter into, including our collaboration with Sanofi, may pose several risks, including the following:

- Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- Collaborators may not perform their obligations as expected.
- The clinical trials conducted as part of these collaborations may not be successful.
- Collaborators may not pursue development and/or commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities.
- Collaborators may delay clinical trials, provide insufficient funding for clinical trials, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing.
- We may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Product candidates developed in collaboration with us may be viewed by any collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates.
- A collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate.

- Disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any programs or product candidates, may cause delays or termination of the research, development, manufacture or commercialization of such programs or product candidates, may lead to additional responsibilities for us with respect to such programs or product candidates or may result in litigation or arbitration, any of which would be time-consuming and expensive. Moreover, in certain circumstances, there could be a misalignment between the contractual obligations given to us by our collaborators and any upstream contractual obligations we may owe to our licensors or other third parties.

- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation. For example, Sanofi has the first right to enforce or defend certain of our intellectual property rights under our collaboration with respect to products in Licensed Fields, and although we may have the right to assume the enforcement and defense of such intellectual property rights if Sanofi does not, our ability to do so may be compromised by Sanofi's actions.

- Disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations.

- Collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability.

- Collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. For example, Sanofi may terminate its collaboration with us for convenience after a specified notice period.

If our collaborations do not result in the successful development and commercialization of products, or if one of any future collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates.

In addition, if any collaborator terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation among the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

We face significant competition in attracting appropriate collaborators to advance the development of any product candidates for which we may seek a collaboration. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator may also have the opportunity to collaborate on other product candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than one with us.

Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical companies has reduced the number of potential future collaborators.

Under the Shire Agreement, prior to the first dosing of a patient with a CFTR MRT Product in a Phase 3 clinical trial, Shire has a 90-day right of first negotiation before we may grant rights or sell assets relating to our CFTR MRT Products to a third party. Shire may exercise the right of first negotiation for a period of 30 days following Shire's receipt of written notice from us notifying Shire of the offer from a third party to acquire, license or commercialize grant rights or sell assets relating to our CF program.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue, which could have an adverse effect on our business, prospects, financial condition and results of operations.

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

We expect to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition, we currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical studies. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to enter into alternative arrangements on commercially reasonable terms, if at all. Switching or including additional third parties involves increased cost and requires management's time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our third parties, we could encounter similar challenges or delays in the future and these challenges or delays could have a material adverse impact on our business, financial condition and prospects.

Our reliance on third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. We and these third parties are required to comply with GCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable regulatory authorities, for all of our products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, clinicaltrials.gov, within certain timeframes. Similar requirements are applicable outside the United States. Failure to comply can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, third parties on whom we rely may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical and preclinical programs. If these third parties do not successfully satisfy 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 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, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products. As a result, our results of operations and the commercial prospects for our products would be harmed, our costs could increase and our ability to generate revenue could be impaired.

Our reliance on third parties to manufacture our product candidates and any future products increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of the product candidates that we are developing or evaluating in our research program. We have limited personnel with experience in drug manufacturing and lack the resources and capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of our product candidates, and we outsource to third parties all manufacturing of our product candidates in preparation for our clinical trials.

In order to conduct clinical trials of our product candidates, we will need to have them manufactured in potentially large quantities. Our third-party manufacturers may be unable to meet this increased demand in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities and at any other time. For example, ongoing data on the stability of our

products may shorten the expiry of our products and lead to clinical trial material supply shortages, and potentially clinical trial delays. If these third-party manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

Our use of new third-party manufacturers increases the risk of delays in production or insufficient supplies of our product candidates as we transfer our manufacturing technology to these manufacturers and as they gain experience manufacturing our product candidates.

Even after a third-party manufacturer has gained significant experience in manufacturing our product candidates or even if we believe we have succeeded in optimizing the manufacturing process, there can be no assurance that such manufacturer will produce sufficient quantities of our product candidates in a timely manner or continuously over time, or at all.

We do not currently have any agreements with third-party manufacturers for the long-term commercial supply of any of our product candidates. In the future, we may be unable to enter into such agreements with third-party manufacturers for commercial supplies of our product candidates, or may be unable to do so on acceptable terms. Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP requirements or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and/or criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP requirements, particularly for the development of mRNA-based therapeutics, and that might be capable of manufacturing for us.

If the third parties that we engage to supply any materials or manufacture product for our preclinical tests and clinical trials should cease to do so for any reason, we likely would experience delays in advancing these tests and trials while we identify and qualify replacement suppliers or manufacturers, and we may be unable to obtain replacement supplies on terms that are favorable to us. For example, we rely on one third-party supplier of the handheld nebulizer that patients in our clinical trials will use to administer MRT5005. The failure of our supplier to provide sufficient quantities, acceptable quality and timely delivery of the nebulizer at an acceptable price, or an interruption in the delivery of goods from such supplier, could delay or otherwise adversely affect our clinical trials of MRT5005, and harm our business and prospects. The use of an alternative manufacturer of the nebulizer could involve significant delays and other costs and regulatory challenges, and may not be available to us on reasonable terms, if at all. In addition, if we are not able to obtain adequate supplies of our product candidates or the substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to the Commercialization of our Product Candidates

If we are unable to establish sales, medical affairs and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.

We do not currently have a sales and marketing organization and have never commercialized a product. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. The establishment and development of our own commercial and medical science liaison teams or the engagement of a contract sales force will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We have entered into a collaboration with Sanofi and may also seek to enter into future collaborations with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many well-funded and profitable pharmaceutical and biotechnology companies that currently have extensive and experienced medical affairs, marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing, sales and medical affairs functions, we may be unable to compete successfully against these more established companies.

Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful. If any of our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals or third-party payors, we will not be able to generate significant revenue from such product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The hospital formulary approval and insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate hospital formulary approval and/or insurance coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

We expect that hospital formulary approval and insurance coverage and reimbursement by government and other third-party payors of our products, if approved, will be essential for most patients to be able to access these treatments. Accordingly, sales of our product candidates, if approved, will depend substantially on the extent to which the costs of our product candidates will be paid by hospitals or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Hospital formulary approval and insurance coverage and reimbursement by other third-party payors may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under the applicable health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient population;
- cost-effective; and
- neither experimental nor investigational.

Obtaining hospital formulary approval and insurance coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that will require us to provide to the hospitals and payors supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to hospital formulary approval and insurance coverage and reimbursement. If hospital formulary approval, insurance coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates.

There is significant uncertainty related to hospital formulary approval and insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. It is difficult to predict what third-party payors will decide with respect to the insurance coverage and reimbursement for our product candidates.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other

countries may use different methods to keep the cost of medical products artificially low. Foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable product revenue.

Moreover, hospitals and government and other third-party payors in the United States and abroad have increasingly taken measures to cap or reduce health care costs. For example, governmental and other third-party payors may attempt to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward reducing hospital costs, managed health care, the increasing influence of health maintenance organizations and additional legislative changes.

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

Even with the requisite approvals from the FDA in the United States, EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates, if approved, will significantly depend on the acceptance of physicians, hospitals and health care payors of our product candidates as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, hospitals, health care payors and others in the medical community. If these commercialized products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of our product candidates over other treatments;
- the cost-effectiveness of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, the EMA or other regulatory body;
- the willingness of physicians to prescribe new therapies over the existing standard of care and future new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning;
- relative convenience and ease of administration;
- our ability to educate the medical community and third-party payors about the benefit of our product candidates;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- any restrictions on the use of our products together with other medications;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor insurance coverage and adequate reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after we begin to commercialize the product.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in foreign economies and markets;
- different pricing and reimbursement regimes;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters, including earthquakes, typhoons, floods and fires.

Risks Related to Our Business Operations

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on members of our executive team. The loss of the services of any of them may adversely impact the achievement of our objectives. Any of our executive officers could leave our employment at any time, as all of our employees are "at-will" employees.

Recruiting and retaining qualified employees, consultants and advisors for our business, including scientific and technical personnel, is also critical to our success. Competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for skilled individuals. In addition, failure to succeed in preclinical studies, clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities and, in the longer term, build a commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- the inability to commercialize any product candidates that we may develop; and
- injury to our reputation and significant negative media attention.

Our insurance coverage may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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

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

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process 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 change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include failures to:

- comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions;
- provide accurate information to the FDA, the EMA and other regulatory authorities;
- comply with health care fraud and abuse laws and regulations in the United States and abroad;
- comply with the U.S. Foreign Corrupt Practices Act, or FCPA, or other anti-corruption laws and regulations;
- comply with U.S. federal securities laws relating to trading in our common stock;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotional practices, as well as sales and customer incentive programs and other business arrangements. Other forms of misconduct could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, EMA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct and expect to implement other internal controls applicable to all of our employees, consultants and contractors, but it is not always possible to identify and deter third-party misconduct, 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 us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, we may be subject to civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government health care programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or

similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could have a significant impact on our business, financial condition, results of operations and prospects.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad or robust, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our products and technology may be adversely affected.

Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and technology. We and our licensors have sought, and intend to seek, to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and technology that are important to our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by such third party, or by the United States Patent and Trademark Office, or USPTO, itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license 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.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we own or may own in the future. We rely, in part, on our outside counsel or our licensing partners to pay these fees due to the USPTO and to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance 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. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our business.

Filing, prosecuting and enforcing patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could 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 from infringing our patents in all countries outside the United States, or from selling or importing products that infringe our patents 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 enforcement is not as strong as that 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.

Even if the patent applications we license or own do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting

such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our product candidates may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full Biologics License Application, or BLA, for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the other company's product. 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. 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 products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, 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.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. The U.S. Supreme Court has ruled on several patent cases in recent years, and these decisions have narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' 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 future decisions by the U.S. Congress, the federal courts and the USPTO, as well as similar bodies in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents and patents we and our licensors or any collaborators may obtain in the future.

Patent reform legislation enacted in the United States in 2011 could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation and switch the U.S. patent system from a "first to invent" system to a "first inventor to file" system. The USPTO has developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular the first inventor to file provisions, became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents, all of which could have a material adverse effect on our business and financial condition.

Our rights to develop and commercialize our product candidates are subject, in part, to the terms and conditions of licenses granted to us by others, and, if we fail to comply with our obligations under these arrangements, we could lose such intellectual property rights or owe damages to the licensor of such intellectual property.

We are a party to several intellectual property license agreements, including agreements with the Massachusetts Institute of Technology, or MIT, that are important to our business, and may need to obtain additional licenses from others to advance our research or allow commercialization of our product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. In that event, we may be required to expend

significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly.

Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, development and commercialization timelines, milestone payments, royalties and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

For example, our license agreement with MIT imposes specified diligence, annual payment, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under the license agreement, MIT may have the right to terminate the license agreement, in which event we might not be able to market, and may be required to transfer to MIT our rights in, any product that is covered by the MIT agreement, including MRT5201 and products that may be developed under our collaboration with Sanofi. Termination of the license agreement may also result in our having to negotiate a new or reinstated license with less favorable terms, which would have a material adverse impact on our business.

In our existing license agreements, and we expect in future agreements, patent prosecution of our licensed technology is in certain cases controlled solely by the licensor, and we are in certain cases required to reimburse the licensor for their costs of patent prosecution. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products covered by the intellectual property. Further, in each of our license agreements, we are responsible for bringing any actions against any third party for infringing the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products and minimum yearly diligence obligations in developing and commercializing the product. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe the intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under any collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. Countering infringement or unauthorized use claims or defending against claims of infringement can be expensive and time-consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or

proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

In addition, many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims 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 own, develop or license.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If we or one of our licensing partners initiates 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 or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. In addition, patent validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term, including a patent term adjustment granted by the USPTO, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions. For example, as of December 31, 2018, two of our patents issued in Europe are under opposition, including one with claims of similar scope as U.S. Patent 10,143,758. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

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, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect, and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of 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, our trade secrets may otherwise become known or be independently discovered by competitors.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of any collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current manufacturing methods, product candidates or future methods or products, resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference proceedings, post grant review and *inter partes* review before the USPTO. The risks of being involved in such litigation and proceedings may also increase as our product candidates approach commercialization and as we gain greater visibility as a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize any of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent.

If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Others may claim an ownership interest in our intellectual property and our product candidates, which could expose us to litigation and have a significant adverse effect on our prospects.

While we are presently unaware of any claims or material assertions by third parties with respect to our patents or other intellectual property, we cannot guarantee that a third party will not assert a claim or an interest in any of such patents or intellectual property. For example, a third party may claim an ownership interest in one or more of our, or our licensors', patents or other proprietary or intellectual property rights. A third party could bring legal actions against us and seek monetary damages or enjoin clinical testing, manufacturing or marketing of the affected product candidate or product. If we become involved in any litigation, it could consume a substantial portion of our resources and cause a significant diversion of effort by our technical and management personnel. If any such action is successful, in addition to any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product candidate or product, in which case we could be required to pay substantial royalties or grant cross-licenses to patents. We cannot, however, assure you that any such license would be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases, which may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.

Trade secrets and know-how can be difficult to protect. To maintain the confidentiality of trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and others upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. Thus, despite such agreement, there can be no assurance that such inventions will not be assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, others may independently discover or develop our trade secrets and proprietary information, and the existence of our own trade secrets affords no protection against such independent discovery. For example, a public presentation in the scientific or popular press on the properties of our product candidates could motivate a third party, despite any perceived difficulty, to assemble a team of scientists having backgrounds similar to those of our employees to attempt to independently reverse engineer or otherwise duplicate our antibody technologies to replicate our success.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals, or we, have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer, or that patents and applications we have filed to protect inventions of these employees, even those related to one or more of our product candidates, are rightfully owned by their former or current employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

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

Any registered trademarks or trade names may be challenged, 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 registered or unregistered trademarks or trade names. Over the long term, if we are unable to 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.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates but that are not covered by the claims of the patents that we own or license or may own in the future;
- we, or any partners or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or any partners or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval process of the FDA is 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 approval by the FDA 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, 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 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 regulatory approval.

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

- the FDA may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA that a product candidate is safe, pure and potent or effective for its proposed indication;
- results of clinical trials may not meet the level of statistical significance required by the FDA for approval;

- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- 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 submission or to obtain regulatory approval in the United States;
- the FDA 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 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, results of operations and prospects. The FDA has substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. 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.

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, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or 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. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drug products are subject to extensive regulation by the FDA, EMA and other regulatory authorities, and regulations may differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of a BLA from the FDA, approval of a marketing authorization application, or MAA, from the EMA, or marketing approval from other applicable regulatory authorities. Our product candidates are in various stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States, Europe or in any other jurisdiction. We have not yet been successful at conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of a BLA and EMA approval of an MAA.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad and may limit our ability to generate revenue from product sales.

In order to market and sell our products in the European Union and many other jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure

varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and any future collaborators and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we or any future collaborators fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we or any future collaborators fail to comply with applicable non-U.S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

We, or any future collaborators, may not be able to obtain and maintain orphan drug exclusivity for our product candidates in the United States and Europe.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In November 2015, the FDA granted orphan drug designation to MRT5005 for the treatment of CF, and in March and June 2018, MRT5201 was granted orphan drug designation for the treatment of OTC deficiency in the U.S. and the EU, respectively. We may seek orphan drug designations for MRT5005 and MRT5201 for other indications or for other of our product candidates. There can be no assurances that we will be able to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate as we have obtained for MRT5005 for the treatment of CF and for MRT5201 for the treatment of OTC deficiency, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and 10 years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Moreover, even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA’s pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug

that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet needs for this condition, the treatment sponsor may apply for FDA fast track designation. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development, regulatory review or approval process with fast track designation compared to conventional FDA procedures. Additionally, 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.

A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate 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 product candidates 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 while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA.

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

Even if we, or any future collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and any future collaborators, will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our third-party manufacturers, any future collaborators and their third-party manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any future collaborators, receive marketing approval for one or more of our product candidates, we, and any future collaborators, and our respective third-party manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to continual requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown side effects or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals, including license revocation;
- refusal to permit the import or export of products;

- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Our relationships with health care providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other health care laws and regulations, which could expose us to civil, criminal and administrative sanctions, contractual damages, reputational harm and diminished future profits and earnings.

Health care providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third-party payors, health care providers and physicians may expose us to broadly applicable fraud and abuse and other health care laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

- *Anti-Kickback Statute*—the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal health care program, such as Medicare and Medicaid;
- *False Claims Act*—the federal civil and criminal false claims laws impose criminal and civil penalties, including, in some cases, through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal health care program or knowingly making a false statement or record material to payment of a false claim or knowingly avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- *HIPAA*—the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any health care benefit program or making false statements relating to health care matters, and apply regardless of the payor (e.g., public or private);
- *HIPAA and HITECH*—HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose obligations on HIPAA covered entities and their business associates, including mandatory contractual terms and required implementation of administrative, physical and technical safeguards to maintain the privacy and security of individually identifiable health information;
- *Transparency Requirements*—federal transparency laws, including the federal Physician Payments Sunshine Act, require applicable manufacturers of covered drugs to annually report payments and other transfers of value to physicians and teaching hospitals and ownership or investment interests held by physicians and their family members; and
- *Analogous State and Foreign Laws*—analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader than similar federal laws, can apply to claims involving health care items or services regardless of payor, and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers or marketing expenditures. 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 pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable health care laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and/or administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion of drugs from government funded health care programs, such as Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect

to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act 2010, or the Bribery Act. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation 2016/679, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also 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. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the health care system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as 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, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the ACA. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of federal health care fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of 2% per fiscal year starting in 2013 and that, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws and any new health care reform measures may result in additional reductions in Medicare and other health care funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provision.

We expect that these health care reforms, as well as other health care reform measures that may be adopted in the future, may result in additional reductions in Medicare, Medicaid and other health care funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare, Medicaid or other government programs may result in a similar reduction in payments from private payors.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the Administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued such payments were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

The cost of prescription pharmaceuticals has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump Administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare

Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly 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.

Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump Administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

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. In addition, regional health care 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 additional state and federal 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 reduced demand for our product candidates or additional pricing pressures.

Finally, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the FCPA, the Bribery Act, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and

relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act, or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements, including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control Laws by U.S., U.K. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

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 significantly harm our business.

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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Although we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

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

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

Risks Related to Ownership of Our Common Stock

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

We believe our executive officers, directors and stockholders which own more than 5% of our outstanding common stock, in the aggregate, beneficially own more than a majority of our capital stock. One of our directors is affiliated with a stockholder who beneficially owns more than 5% of our outstanding common stock. If these stockholders were to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and business affairs. For example, these persons, if they act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in management of our company that other stockholders disagree with.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is performing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below.

Moreover, holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Furthermore, in July 2018, we registered all shares of common stock that we may issue under our equity compensation plans. Registered shares can be freely sold in the public market, subject only to volume limitations applicable to affiliates. Sales of a substantial number of shares of our common stock, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely, in part, on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. A lack of research coverage or adverse coverage may negatively impact the market price of our common stock. In addition, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

The price of our common stock is volatile and may fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price is volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- results of preclinical studies and clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- commencement or termination of collaborations;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;

- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of health care payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- the entry into significant acquisitions, strategic partnerships or divestitures by us or our competitors;
- significant sales of our common stock, including sales by our directors, executive officers or 5% stockholders;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

If any of the foregoing matters were to occur, or if our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on the Nasdaq Global Select Market on June 28, 2018. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price for our common stock and thereby affect the ability of our stockholders to sell their shares. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an EGC until the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date or our initial public offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the last day of the first fiscal year in which the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved; and
- an exemption from compliance with the requirement of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements.

In addition, the JOBS Act provides that an EGC may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not EGCs.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations, such as an exemption from providing selected financial data and an ability to provide simplified executive compensation information and only two years of audited financial statements.

We have elected to take advantage of certain of the reduced reporting obligations. Investors may find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and requirements.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and the Nasdaq Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal control over financial reporting that are deemed to be significant deficiencies or material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, continue to engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We previously identified a material weakness in our internal control over financial reporting, which has been remediated. If we identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business and stock price.

We previously identified a material weakness in our internal control over financial reporting that was unremediated as of December 31, 2017. Although this material weakness was remediated as of December 31, 2018, we cannot assure that we may not identify another material weakness in the future. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

In preparation of our financial statements to meet the requirements of our initial public offering, we determined that a material weakness in our internal control over financial reporting existed during fiscal 2016 and remained unremediated as of December 31, 2017. The material weakness we identified is that we did not design and maintain effective controls and procedures over our accounting for and reporting of the income tax impacts of business combinations. This control deficiency could result in a misstatement of our accounts or disclosures that would result in a material misstatement of our annual or interim condensed consolidated financial statements that would not be prevented or detected, and accordingly, we determined that the control deficiency constitutes a material weakness. The material weakness also resulted in revisions to our previously issued 2016 annual consolidated financial statements, which we concluded were not material to those financial statements, and adjustments to our interim condensed consolidated financial statements for the nine months ended September 30, 2017 before their issuance. Specifically, the material weakness resulted in errors in our accounting for and reporting of income taxes and goodwill in the purchase accounting for a business combination and in subsequent reporting periods.

We cannot assure you that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent or avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or identify any additional material weaknesses in the future, or otherwise fail to maintain an effective system of internal controls, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our share price may decline as a result.

Provisions in our certificate of incorporation and bylaws and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or stockholders.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by our directors, officers, other employees or stockholders to the company or our stockholders, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware, or any action asserting a claim arising pursuant to our certificate of incorporation or our bylaws or governed by the internal affairs doctrine. This provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, other employees or other stockholders, which may discourage such lawsuits against us and our directors, officers, other employees or other stockholders. Alternatively, if a court were to find this provision in our 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 adversely affect our business and financial condition.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future, and investors seeking cash dividends should not purchase shares of our common stock.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal facilities consist of office and laboratory space. We occupy approximately 59,000 square feet of office and laboratory space in Lexington, Massachusetts under a 10-year lease agreement we entered into in June 2017. We occupied this leased property as our headquarters in March 2018. This lease expires in April 2028, and we have two five-year options to extend it through April 2038. We believe this office and laboratory space will be sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

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 for Our Common Stock

Our common stock trades under the symbol "TBIO" on the Nasdaq Global Select Market and has been publicly traded since June 28, 2018. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 14, 2019, there were approximately 97 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Use of Proceeds from Registered Securities

On July 2, 2018, we closed our IPO of 9,350,000 shares of common stock at a public offering price of $13.00 per share, and on July 24, 2018, we issued and sold an additional 364,371 shares of common stock at a price of $13.00 per share pursuant to the exercise of the underwriters' over-allotment option. The aggregate gross proceeds to us from our IPO, inclusive of the over-allotment exercise, were $126.3 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to registration statement on Form S-1 (File No. 333-225368), which was declared effective by the SEC on June 27, 2018. Citigroup Global Markets Inc., Leerink Partners LLC and Evercore Group L.L.C. acted as joint book-running managers for the offering and as representatives of the underwriters. The offering commenced on June 27, 2018 and did not terminate until the sale of all of the shares offered.

Aggregate net proceeds from the offering, inclusive of the proceeds from the over-allotment exercise, were $113.2 million, after deducting underwriting discounts and commissions of $8.8 million and estimated offering expenses of $4.3 million payable by us. None of the underwriting discounts and commissions or offering expenses were paid directly or indirectly to any directors or officers of ours or their associates or to persons owning 10% or more of any class of equity securities or to any affiliates of ours.

As of December 31, 2018, we have used approximately $20.9 million of the net proceeds to fund the development of MRT5005 and MRT5201, to fund the discovery and additional preclinical research and development of additional product candidates and platform enhancement, and for working capital and other general corporate purposes. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC on June 29, 2018 pursuant to Rule 424(b) under the Securities Act.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other financial information included in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements, which are included at the end of this Annual Report on Form 10-K. Our historical results are not necessarily indicative of results that should be expected in any future period.

	Year Ended December 31,		
	2018	2017	2016
	(in thousands, except per share amounts)		
Consolidated Statement of Operations Data:			
Collaboration revenue	$ 1,420	$ —	$ —
Operating expenses:			
Research and development	58,024	47,023	15,658
General and administrative	22,606	14,311	11,144
Change in fair value of contingent consideration	25,020	17,914	—
Total operating expenses	105,650	79,248	26,802
Loss from operations	(104,230)	(79,248)	(26,802)
Other income (expense):			
Interest income	1,323	281	114
Other income (expense), net	(53)	43	(10)
Total other income (expense), net	1,270	324	104
Loss before benefit from income taxes	(102,960)	(78,924)	(26,698)
Benefit from income taxes	5,565	12,481	—
Net loss	(97,395)	(66,443)	(26,698)
Accretion of redeemable convertible preferred stock to redemption value	(644)	(719)	(671)
Net loss attributable to common stockholders	$ (98,039)	$ (67,162)	$ (27,369)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.64)	$ (8.66)	$ (18.14)
Weighted average common shares outstanding—basic and diluted	26,945,508	7,756,180	1,509,048

(1) See Note 13 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

	As of December 31,	
	2018	2017
	(in thousands)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 144,103	$ 58,055
Working capital(1)	135,315	50,950
Total assets	287,651	198,547
Contingent consideration liability	103,642	81,009
Deferred revenue	44,413	—
Redeemable convertible preferred stock	—	192,896
Total stockholders' equity (deficit)	125,295	(93,515)

(1) We define working capital as current assets less current liabilities.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and at the end of this report, including those set forth under Item 1A. "Risk Factors" in this Annual Report on Form 10-K.

Overview

We are a clinical-stage messenger RNA, or mRNA, therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction. Using our proprietary mRNA therapeutic platform, or MRT platform, we create mRNA that encodes functional proteins. We believe that the mRNA design, delivery and manufacturing capabilities of our MRT platform provide us with the most advanced platform for developing product candidates that deliver mRNA encoding functional proteins for therapeutic uses. Our mRNA is delivered to the target cell where the cell's own machinery recognizes it and translates it, restoring or augmenting protein function to treat or prevent disease. We believe that our MRT platform is broadly applicable across multiple diseases in which the production of a desirable protein can have a therapeutic effect. We are initially focused on restoring the expression of intracellular and transmembrane proteins, areas that have eluded conventional protein therapeutics, in patients with genetic diseases where there is high unmet medical need.

We are developing our lead MRT product candidate for the lung, MRT5005, for the treatment of cystic fibrosis, or CF. We are conducting a Phase 1/2 clinical trial to evaluate the safety and efficacy of MRT5005 and anticipate reporting interim data from this trial in the second half of 2019. We are developing our lead MRT product candidate for the liver, MRT5201, for the treatment of ornithine transcarbamylase, or OTC, deficiency. In December 2018, we submitted an investigational new drug application, or IND, for MRT5201, which the U.S. Food and Drug Administration, or FDA, has placed on clinical hold. The FDA is requiring additional preclinical toxicology data. We have identified the additional preclinical studies required, and plan to complete these studies and submit a response to the FDA in the fourth quarter of 2019. Additionally, we intend to leverage the broad applicability of our platform by identifying lead preclinical candidates for additional lung and liver disease targets, and through a collaboration with Sanofi Pasteur Inc., or Sanofi, the vaccines global business unit of Sanofi S.A., to develop infectious disease vaccines using mRNA technology for up to five infectious disease pathogens. We have several discovery-stage programs to identify additional potential mRNA therapeutic candidates. We believe that our MRT platform is distinct from other mRNA-based technologies and has the potential to provide clinical benefits by transforming life-threatening illnesses into manageable chronic conditions.

Since our inception in 2011, we have devoted substantially all of our focus and financial resources to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights and conducting discovery, research and development activities for our programs. We do not have any products approved for sale and have not generated any revenue from product sales.

On June 27, 2018, our registration statement on Form S-1 relating to our initial public offering of our common stock, or the IPO, was declared effective by the Securities and Exchange Commission, or SEC. In the IPO, which closed on July 2, 2018, we issued and sold 9,350,000 shares of common stock at a public offering price of $13.00 per share. On July 24, 2018, we issued and sold an additional 364,371 shares of common stock at a price of $13.00 per share pursuant to the exercise of the underwriters' over-allotment option. The aggregate net proceeds we received from the IPO, inclusive of the proceeds from the over-allotment exercise, were $113.2 million after deducting underwriting discounts and commissions of $8.8 million and offering expenses of $4.3 million. Upon closing of the IPO, all 142,288,292 shares of our redeemable convertible preferred stock then outstanding converted into an aggregate of 25,612,109 shares of common stock.

On June 8, 2018, we entered into a collaboration and license agreement, or the Sanofi Agreement, with Sanofi to develop mRNA vaccines for up to five infectious disease pathogens. The Sanofi Agreement became effective on July 9, 2018. Under the Sanofi Agreement, we and Sanofi will jointly conduct research and development activities to advance mRNA vaccines and mRNA vaccine platform development during a three-year research term, which may be extended by mutual agreement. We are eligible to receive up to $805.0 million in payments, which includes an upfront payment of $45.0 million, which we received in July 2018, certain development, regulatory and sales-related milestones across several vaccine targets, and option exercise fees if Sanofi exercises its option related to development of vaccines for additional pathogens. We are also eligible to receive tiered royalty payments associated with worldwide sales of the developed vaccines, if any.

We have funded our operations primarily with proceeds from the sale of redeemable convertible preferred stock and the sale of bridge units, which ultimately converted into shares of our preferred stock, the proceeds from our IPO and an upfront payment received under the Sanofi Agreement. Through December 31, 2018, we had received net cash proceeds of $113.2 million from our

IPO, net cash proceeds of $189.2 million from sales of our preferred stock and bridge units and $45.0 million in an upfront payment from Sanofi.

Since our inception, we have incurred significant operating losses. Our ability to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates. Our net losses were $97.4 million and $66.4 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $246.2 million. We expect to continue to incur significant expenses for at least the next several years as we advance our product candidates from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties or grants from organizations and foundations. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

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 we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2018, we had cash, cash equivalents and short-term investments of $144.1 million. We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. In accordance with the requirements of Accounting Standards Update, or ASU, No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, or ASC 205-40, we have determined that there is substantial doubt about our ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations. If we are unable to obtain funding, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could adversely affect our business prospects, and we may be unable to continue operations. See "—Liquidity and Capital Resources—Funding Requirements."

Acquisition of MRT Program

On December 22, 2016, we entered into an asset purchase agreement with Shire Human Genetic Therapies, Inc., or Shire, a subsidiary of Shire plc, which, as amended on June 7, 2018, we refer to as the Shire Agreement. Pursuant to the Shire Agreement, we acquired Shire's mRNA therapy platform, or the MRT Program, for an aggregate purchase price of $112.2 million, consisting of 5,815,560 shares of common stock with an aggregate fair value of $41.1 million and contingent consideration with a fair value of $71.1 million on the acquisition date. The contingent consideration includes the obligation to issue additional shares of common stock to Shire in connection with the closing of subsequent equity financings required under the terms of the Shire Agreement, which had a fair value of $8.4 million on the acquisition date, as well as the obligation to make future milestone and earnout payments upon the occurrence of specified commercial milestones, which had a fair value of $62.7 million on the acquisition date. As of December 31, 2018, we have fully satisfied our obligation to issue shares of common stock to Shire under the Shire Agreement. Under the Shire Agreement, we are obligated to use commercially reasonable efforts to develop and seek and obtain regulatory approval for products that include or are composed of MRT compounds acquired from Shire, or MRT Products, and to achieve specific developmental milestones.

In June 2017, we implemented a strategy to primarily devote our resources to the advancement of our MRT platform. Thereafter, we then devoted substantially fewer resources to the advancement of our oligonucleotide discovery program, which seeks to develop RNA-targeted product candidates that selectively upregulate gene expression to increase endogenous protein levels for

therapeutic benefit. We expect to continue to primarily devote our resources to the advancement of our MRT platform for the foreseeable future.

Components of Our Results of Operations

Revenue from Product Sales

To date, we have not generated any revenue from product sales, and we do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales.

Collaboration Revenue

In June 2018, we entered into the Sanofi Agreement, a collaboration and license agreement with Sanofi to develop mRNA vaccines and mRNA vaccine platform development for up to five infectious disease pathogens, or the Licensed Fields. The Sanofi Agreement became effective in July 2018.

Under the terms of the Sanofi Agreement, we have granted to Sanofi exclusive, worldwide licenses under applicable patents, patent applications, know-how and materials, including those arising under the collaboration, to develop, commercialize and manufacture mRNA vaccines to prevent, treat or cure diseases, disorders or conditions in humans caused by any of three Licensed Fields. In addition, pursuant to the terms of the Sanofi Agreement and subject to certain limitations, Sanofi has options to add up to two additional infectious disease pathogens within the granted licenses to the Licensed Fields.

Under revenue recognition guidance, we account for: (i) the license we conveyed to Sanofi with respect to the Licensed Fields, (ii) the licensed know-how to be conveyed to Sanofi with respect to the Licensed Fields, (iii) our obligations to perform research and development on the Licensed Fields, (iv) our obligation to transfer licensed materials to Sanofi, (v) our obligation to manufacture and supply certain non-clinical and clinical mRNA vaccines and materials containing mRNA until we transfer such manufacturing capabilities to Sanofi and (vi) the technology and process transfer as a single performance obligation. We recognize revenue using the cost-to-cost input method, which we believe best depicts the transfer of control to the customer. Under the cost-to-cost input method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified performance obligation. Under this method, revenue is recorded as a percentage of the estimated transaction price based on the extent of progress towards completion.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the discovery and development of our product candidates. We expense research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with third parties, such as consultants and contract research organizations, or CROs;
- the cost of manufacturing drug products for use in our preclinical studies and clinical trials, including under agreements with third parties, such as consultants and contract manufacturing organizations, or CMOs;
- laboratory supplies;
- facilities, depreciation and other expenses, which include direct or allocated expenses for rent and maintenance of facilities and insurance;
- costs to fulfill our obligations under the Sanofi Agreement;
- costs related to compliance with regulatory requirements; and

- payments made under third-party licensing agreements.

We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense when the services have been performed or the goods have been delivered, or when it is no longer expected that the goods will be delivered or the services rendered. Upfront payments, milestone payments (other than those deemed contingent consideration in a business combination) and annual maintenance fees under license agreements are expensed in the period in which they are incurred.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to outside consultants, CROs, CMOs and central laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct research and development expenses by program also include costs of laboratory supplies incurred for each program as well as fees incurred under license agreements. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to conduct our research and discovery and to manage our preclinical development, process development, manufacturing and clinical development activities.

The table below summarizes our research and development expenses incurred by program:

	Year Ended December 31,	
	2018	2017
	(in thousands)	
CF program (including MRT5005)	$ 18,270	$ 15,641
OTC deficiency program (including MRT5201)	10,225	8,244
MRT discovery program	6,186	2,560
Vaccine discovery program	373	—
Oligonucleotide discovery program	134	2,499
Unallocated research and development expenses	22,836	18,079
Total research and development expenses	$ 58,024	$ 47,023

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years as we conduct our clinical trials of MRT5005 for the treatment of patients with CF; conduct additional preclinical studies to support our IND for MRT5201, and if the FDA's clinical hold is lifted, conduct clinical trials for MRT5201; conduct research and development activities to advance mRNA vaccines and develop an mRNA vaccine platform under the Sanofi Agreement; prepare regulatory filings for our product candidates; continue to discover and develop additional product candidates; and potentially advance product candidates from our MRT platform into later stages of clinical development. We expect to continue to devote a substantial portion of our resources to our MRT platform for the foreseeable future.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- establishing an appropriate safety profile with IND-enabling studies;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt of regulatory approvals from applicable regulatory authorities;

- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- our ability to establish new licensing or collaboration arrangements;
- the success of our collaboration with Sanofi;
- the performance of our future collaborators, if any;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials and for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, in December 2018, we submitted an IND to the FDA supporting the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. Subsequently, the FDA notified us that our IND for MRT5201 was placed on clinical hold. In addition, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that product candidate. We may never obtain regulatory approval for any of our product candidates. Drug commercialization will take several years and millions of dollars in development costs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative expenses also include facilities, depreciation and other expenses, which include direct or allocated expenses for rent and maintenance of facilities and insurance, as well as professional fees for legal, patent, consulting, investor and public relations, accounting and audit services.

We anticipate that our general and administrative expenses will increase compared to 2018 as we anticipate increased accounting, audit, legal, regulatory, compliance, director and officer insurance and investor and public relations costs associated with being a public company.

Change in Fair Value of Contingent Consideration

In connection with our acquisition of the MRT Program, we recognized contingent consideration liabilities for future potential milestone and earnout payment obligations and, prior to the IPO, anti-dilution rights with respect to common stock issued to Shire. The contingent consideration was initially recorded at fair value on the acquisition date and is subsequently remeasured to fair value at each reporting date. Any changes in the fair value of the contingent consideration liabilities are recognized as operating income or expenses.

Other Income (Expense), Net

Interest Income

Interest income consists of income recognized in connection with our investments in money market funds and U.S. government agency bonds.

Other Income (Expense), Net

Other income (expense), net consists of miscellaneous income and expense unrelated to our core operations.

Income Taxes

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the Tax Act. The Tax Act includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from a top marginal rate of 35% to a flat rate of 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks.

We recognized an income tax benefit of $5.6 million and $12.5 million during the years ended December 31, 2018 and 2017, respectively. The $5.6 million income tax benefit recognized during the year ended December 31, 2018, resulted from a reduction in the deferred tax liabilities recorded as part of our acquisition of the MRT Program. The $12.5 million income tax benefit recognized during the year ended December 31, 2017 consisted of (i) a $6.4 million benefit due to a reduction of the same amount in the deferred tax liabilities recorded as part of our acquisition of the MRT Program and (ii) a $6.1 million benefit resulting from the impact of the Tax Act.

During 2017, we recorded tax charges for the impact of the Tax Act effects using the current available information and technical guidance on the interpretations of the Tax Act. As permitted by the SEC Staff Accounting Bulletin 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act, we recorded provisional estimates and have subsequently finalized our accounting analysis based on the guidance, interpretations and data available as of December 31, 2018 with no material changes to our initial estimates.

As of December 31, 2018, we had U.S. federal net operating loss carryforwards of $190.8 million, of which $122.1 million will, if not utilized, begin to expire in 2031. As of December 31, 2018, we had U.S. state net operating loss carryforwards of $171.7 million, which will, if not utilized, begin to expire in 2031. As of December 31, 2018, we also had U.S. federal and state research and development tax credit carryforwards of $5.1 million and $2.0 million, respectively, which will, if not utilized, begin to expire in 2032 and 2028, respectively, and orphan drug tax credit carryforwards of $6.6 million, which begin to expire in 2037. We also have state investment tax credit carryforwards of $0.4 million, which will, if not utilized, begin to expire in 2019. As of December 31, 2018, we recorded a full valuation allowance against our deferred tax assets, except for $0.8 million related primarily to indefinite-lived net operating loss carryforwards. As of December 31, 2017, we recorded a full valuation allowance against our deferred tax assets, except for $2.4 million of deferred tax assets related to deductible temporary differences that will generate unlimited net operating loss carryforwards when they reverse in future periods.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	Change
	(in thousands)		
Collaboration revenue	$ 1,420	$ —	$ 1,420
Operating expenses:			
Research and development	58,024	47,023	11,001
General and administrative	22,606	14,311	8,295
Change in fair value of contingent consideration	25,020	17,914	7,106
Total operating expenses	105,650	79,248	26,402
Loss from operations	(104,230)	(79,248)	(24,982)
Other income (expense):			
Interest income	1,323	281	1,042
Other income (expense), net	(53)	43	(96)
Total other income (expense), net	1,270	324	946
Loss before benefit from income taxes	(102,960)	(78,924)	(24,036)
Benefit from income taxes	5,565	12,481	(6,916)
Net loss	$ (97,395)	$ (66,443)	$ (30,952)

Collaboration Revenue

Collaboration revenue was $1.4 million for the year ended December 31, 2018, which was derived from the Sanofi Agreement. There was no collaboration revenue recognized in the year ended December 31, 2017.

Research and Development Expenses

	Year Ended December 31,		
	2018	2017	Change
	(in thousands)		
Direct research and development expenses by program:			
CF program (including MRT5005)	$ 18,270	$ 15,641	$ 2,629
OTC deficiency program (including MRT5201)	10,225	8,244	1,981
MRT discovery program	6,186	2,560	3,626
Vaccine discovery program	373	—	373
Oligonucleotide discovery program	134	2,499	(2,365)
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	14,721	11,385	3,336
Other	8,115	6,694	1,421
Total research and development expenses	$ 58,024	$ 47,023	$ 11,001

Research and development expenses were $58.0 million for the year ended December 31, 2018, compared to $47.0 million for the year ended December 31, 2017. The increase of $11.0 million was primarily due to increases in external research and development service costs resulting from the continued development of our CF and OTC deficiency programs, an increase in spending on our MRT discovery program as well as an increase in personnel-related costs, partially offset by a decrease in our oligonucleotide discovery program.

Direct expenses of our CF program increased by $2.6 million in the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to increased clinical trial costs related to our Phase 1/2 clinical trial of MRT5005 for the treatment of patients with CF as well as increased manufacturing and raw material costs.

Direct expenses of our OTC deficiency program increased by $2.0 million in the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to increased manufacturing activities as well as the initial costs of CROs to conduct our planned Phase 1/2 clinical trial of MRT5201 for the treatment of patients with OTC deficiency, which was placed on clinical hold in January 2019 while we conduct additional preclinical studies.

Direct expenses of our MRT discovery program increased by $3.6 million in the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to increased costs related to our ongoing exploratory research in the program.

Direct expenses of our vaccine discovery program increased by $0.4 million in the year ended December 31, 2018 compared to the year ended December 31, 2017 as a result of the Sanofi Agreement which became effective in July 2018. The expenses in the year ended December 31, 2018 were related to our exploratory research in the program.

Direct expenses of our oligonucleotide discovery program decreased by $2.4 million in the year ended December 31, 2018 compared to the year ended December 31, 2017 due to a shift in our focus from the oligonucleotide discovery program to our MRT platform in June 2017.

Unallocated research and development expenses increased by $4.8 million in the year ended December 31, 2018 compared to the year ended December 31, 2017. The increase of $3.3 million in personnel-related costs was primarily due to an increase in stock-based compensation expense, resulting from options granted during the years ended December 31, 2018 and 2017. Additionally, there was an increase in headcount during the year ended December 31, 2018 compared to the same period in 2017. The increase of $1.4 million in other unallocated research and development expenses was primarily due to a $0.7 million payment owed to the Massachusetts Institute of Technology, or MIT, as its share of sublicense income with respect to the upfront payment received under the Sanofi Agreement and $0.4 million of amortization expense recorded in the year ended December 31, 2018 related to the definite-lived in-process research and development, or IPR&D, MRT intangible asset. Upon commencement of the Sanofi Agreement, the IPR&D - MRT intangible asset was reclassified from indefinite-lived to definite-lived intangible assets and we began amortization of this intangible asset.

General and Administrative Expenses

General and administrative expenses were $22.6 million for the year ended December 31, 2018, compared to $14.3 million for the year ended December 31, 2017. The increase of $8.3 million was primarily due to increases of $3.7 million in personnel-related costs, $2.0 million in professional fees, $0.7 million in depreciation expense and $0.6 million in insurance costs.

The $3.7 million increase in personnel-related costs was primarily due to an increase in stock-based compensation expense, resulting from options granted during the years ended December 31, 2018 and 2017, as well as an increase in headcount in the year ended December 31, 2018 compared to the same period in 2017.

The $2.0 million increase in professional fees was due to an increase in legal fees primarily associated with filing patent applications and prosecuting our intellectual property portfolio.

The $0.7 million increase in depreciation expense was primarily due to the acceleration of unamortized leasehold improvements related to the real estate lease we acquired in connection with our acquisition of the MRT Program in December 2016 which we surrendered in June 2018.

The $0.6 million increase in insurance costs was a result of additional insurance coverage associated with operating as a public company.

Change in Fair Value of Contingent Consideration

In the years ended December 31, 2018 and 2017, we recognized operating expenses of $25.0 million and $17.9 million, respectively, for changes in the fair value of the contingent consideration liabilities we recorded in connection with our acquisition of the MRT Program in December 2016. The contingent consideration liabilities relate to future potential milestone and earnout payment obligations and, prior to the IPO, anti-dilution rights with respect to common stock issued to Shire. The $7.1 million increase in the expense was attributed primarily to an increase in the fair value of the contingent consideration liability for future earnout payments that could be due. The increase in the fair value of contingent consideration during the year ended December 31, 2018 was primarily due to the continued progress of MRT5005, including the initiation in May 2018 of our Phase 1/2 clinical trial of MRT5005 for the treatment of patients with CF, the continued advancement of MRT5201 for the treatment of patients with OTC deficiency, the IND for which has been placed on clinical hold by the FDA, the time value of money due to the passage of time, as well as a decrease in the discount rate.

Benefit from Income Taxes

During the years ended December 31, 2018 and 2017, we recognized income tax benefits of $5.6 million and $12.5 million, respectively. The $5.6 million income tax benefit recognized during the year ended December 31, 2018, resulted from a reduction in the deferred tax liabilities recorded as part of our acquisition of the MRT Program. The $12.5 million income tax benefit recognized during the year ended December 31, 2017 consisted of (i) a $6.4 million benefit due to a reduction of the same amount in the deferred tax liabilities recorded as part of our acquisition of the MRT Program and (ii) a $6.1 million benefit resulting from the impact of the Tax Act.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue from product sales, generated limited revenue from the Sanofi Agreement and have incurred significant operating losses and negative cash flows from our operations. We have not yet commercialized any of our product candidates, and we do not expect to generate revenue from sales of any product candidates for several years, if at all. See "—Funding Requirements" and Note 1 to the consolidated financial statements appearing at the end of this Annual Report on Form 10-K for a further discussion of our liquidity and the conditions and events that raise substantial doubt regarding our ability to continue as a going concern.

We have funded our operations primarily with proceeds from the sale of redeemable convertible preferred stock and the sale of bridge units, which ultimately converted into shares of our preferred stock, the proceeds from our IPO and an upfront payment received under the Sanofi Agreement. Through December 31, 2018, we had received net cash proceeds of $113.2 million from our IPO, net cash proceeds of $189.2 million from sales of our preferred stock and bridge units and $45.0 million in an upfront payment from Sanofi.

On June 27, 2018, our registration statement on Form S-1 relating to our IPO was declared effective by the SEC. In the IPO, which closed on July 2, 2018, we issued and sold 9,350,000 shares of common stock at a public offering price of $13.00 per share. On July 24, 2018, we issued and sold an additional 364,371 shares of common stock at a price of $13.00 per share pursuant to the exercise of the underwriters' over-allotment option. The aggregate net proceeds we received from the IPO, inclusive of the proceeds from the over-allotment exercise, were $113.2 million after deducting underwriting discounts and commissions of $8.8 million and offering expenses of $4.3 million. Upon closing of the IPO, all 142,288,292 shares of our redeemable convertible preferred stock then outstanding converted into an aggregate of 25,612,109 shares of common stock.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2018	2017
	(in thousands)	
Net cash used in operating activities	$ (22,133)	$ (50,788)
Net cash provided by (used in) investing activities	(85,290)	304
Net cash provided by financing activities	113,623	41,747
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 6,200	$ (8,737)

Operating Activities

During the year ended December 31, 2018, operating activities used $22.1 million of cash, resulting from our net loss of $97.4 million, partially offset by net cash provided by changes in our operating assets and liabilities of $45.6 million and net non-cash charges of $29.6 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2018 included a $43.6 million increase in deferred revenue resulting from the $45.0 million received under Sanofi Agreement, which became effective in July 2018. Net non-cash charges for the year ended December 31, 2018 primarily consisted of a $25.0 million increase in the change in the fair value of contingent consideration which was primarily due to the continued progress of MRT5005, including the initiation in May 2018 of our Phase 1/2 clinical trial of MRT5005 for the treatment of patients with CF, the continued advancement of MRT5201 for the treatment of patients with OTC deficiency, the IND for which has been placed on clinical hold by the FDA, the time value of money due to the passage of time, as well as a decrease in the discount rate.

During the year ended December 31, 2017, operating activities used $50.8 million of cash, resulting from our net loss of $66.4 million, partially offset by net non-cash charges of $10.6 million and net cash provided by changes in our operating assets and liabilities of $5.0 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2017 consisted primarily of a $4.0 million increase in accounts payable, a $2.3 million increase in accrued expenses and a $1.0 million increase in deferred rent, all partially offset by a $2.3 million increase in prepaid expenses and other assets. The increases in accounts payable and accrued expenses were primarily due to the increases in research and development activities and costs associated with our MRT platform as well as personnel-related costs due to an increase in headcount in 2017 compared to 2016. The increase in prepaid expenses and other assets was primarily due to increased prepaid amounts paid to CMOs for manufacturing drug product materials and CROs for research contracts related to our MRT platform. The increase in deferred rent was due to a facilities lease we entered into in June 2017 for office and laboratory space in Lexington, Massachusetts.

Investing Activities

During the year ended December 31, 2018, net cash used in investing activities was $85.3 million, consisting of $136.7 million of purchases of short-term investments as well as $6.6 million of purchases of property and equipment, which primarily consisted of leasehold improvements and other property and equipment related to the lease of our new headquarters in Lexington, Massachusetts, partially offset by $58.0 million of sales and maturities of short-term investments.

During the year ended December 31, 2017, net cash provided by investing activities was $0.3 million, consisting of $73.8 million of sales and maturities of short-term investments, partially offset by $70.8 million of purchases of short-term investments and $2.8 million of purchases of property and equipment.

Financing Activities

During the year ended December 31, 2018, net cash provided by financing activities was $113.6 million, consisting of, in part, net proceeds from our IPO, inclusive of the proceeds from the over-allotment exercise, of $113.3 million after deducting underwriting discounts and commissions and offering expenses.

During the year ended December 31, 2017, net cash provided by financing activities was $41.7 million, consisting of gross proceeds of $42.0 million from our sale of Series C preferred stock in December 2017, net of $0.1 million of issuance costs, partially offset by $0.2 million of payments of initial public offering costs.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue ongoing and initiate new clinical trials of and seek marketing approval for our product candidates. In addition, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if, and as, we:

- leverage our programs to advance our other product candidates into preclinical and clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- seek to discover and develop additional product candidates;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- hire additional clinical, quality control and scientific personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

We believe that our existing cash, cash equivalents and short-term investments of $144.1 million as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. In accordance with the requirements of ASC 205-40, based on our recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations.

We will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic and market conditions, many of which are outside of our control, and we may be unable to raise financing when needed, or on terms favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which could adversely affect our business prospects, and we may be unable to continue our operations. Factors that may affect our planned future capital requirements and accelerate our need for additional working capital include the following:

- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the ability to receive additional non-dilutive funding, including grants from organizations and foundations;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;

- the cost and timing of hiring new employees to support our continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the ability to establish and maintain collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties and grants from organizations and foundations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders may be materially diluted, and the terms of such securities could include liquidation or other preferences that could adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, debt financing would result in increased fixed payment obligations.

If we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2018 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less Than 1 Year	1 to 3 Years	4 to 5 Years	More Than 5 Years
	(in thousands)				
Operating lease commitments(1)	$ 26,549	$ 2,534	$ 5,298	$ 5,621	$ 13,096
Purchase commitments(2)	23,975	9,562	3,943	6,980	3,490
Research commitments(3)	712	712	—	—	—
License agreement obligations(4)	1,100	150	350	400	200
Total	$ 52,336	$ 12,958	$ 9,591	$ 13,001	$ 16,786

(1) Reflects minimum payments due under our operating lease for office and laboratory space, which expires April 2028.
(2) Reflects minimum purchase commitments under a master supply agreement expiring in December 2024 with Roche Diagnostics Corporation, which we engaged to manufacture drug product materials.
(3) Reflects sponsored research commitments under our research agreement with MIT, which expires October 2019.
(4) Reflects the annual license maintenance fees payable under our license agreement with MIT. Amounts in the table represent reflect such fees payable through 2024, but we will be obligated to make such payments until the license agreement is terminated.

In addition, under various licensing and related agreements to which we are a party, we may be required to make milestone and earnout payments and to pay royalties and other amounts to third parties. We have not included any such contingent payment obligations in the table above as the amount, timing and likelihood of such payments are not known. Such contingent payment obligations are described below.

Under the Shire Agreement, as amended, we are obligated to make milestone payments to Shire of up to $60.0 million in the aggregate upon the occurrence of specified commercial milestones, including upon the first commercial sale of an MRT Product for

the treatment of CF and upon the achievement of a specified level of annual net sales with respect to an MRT Product. We are also obligated to make additional milestone payments of $10.0 million for each non-CF MRT Product upon the first commercial sale of a non-CF MRT Product; provided that such milestone payments will only be due once for any two non-CF MRT Products that contain the same MRT compounds or once per non-CF MRT Product that is a vaccine developed under our collaboration with Sanofi. Under the Shire Agreement, we are also obligated to pay a quarterly earnout payment of a mid-single-digit percentage of net sales of each MRT Product. The earnout period, which is determined on a product-by-product and country-by-country basis, will begin on the date of the first commercial sale of such MRT Product in such country and will end on the later of (1) 10 years after such first commercial sale and (2) the expiration of the last valid claim of the patent rights acquired from Shire or derived from patent rights or know-how acquired from Shire covering such MRT Product in such country.

We and Shire entered into an amendment to the asset purchase agreement on June 7, 2018 to align certain terms of the asset purchase agreement with the Sanofi Agreement, which we entered into with Sanofi on June 8, 2018.

Under our license agreement with MIT, we are obligated to make milestone payments to MIT aggregating up to $1.375 million upon the achievement of specified clinical and regulatory milestones with respect to each licensed product and $1.250 million upon our first commercial sale of each licensed product, and to pay royalties of a low-single-digit percentage to MIT based on our, and any of our affiliates' and sublicensees', net sales of licensed products. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances. In addition, we are obligated to pay MIT a low-double-digit percentage of the portion of income from sublicensees that we ascribe to the MIT-licensed patents, excluding royalties on net sales and research support payments. In 2019, pursuant to such provision, we have agreed to pay $0.7 million to MIT as its share of sublicense income with respect to the upfront payment received under the Sanofi Agreement, which is included in accrued expenses in our consolidated balance sheet as of December 31, 2018. The amounts that we may owe to MIT will depend upon the relative value of the patents we licensed from MIT and sublicensed to Sanofi as compared to the other rights that we licensed to Sanofi. The determination of the relative value of such rights is subject to a process described in our license agreement with MIT.

Under the Sanofi Agreement, we and Sanofi have agreed to collaborate to perform certain research and development activities to advance mRNA vaccines and mRNA vaccine platform development during a three-year research term, which may be extended by mutual agreement. Under the Sanofi Agreement, if we commercialize any product covered by a Sanofi patent right, we will be required to pay to Sanofi a royalty of a low-single-digit percentage. The amount, timing and likelihood of such payments are not known.

We have entered into contracts in the normal course of business with CROs, CMOs and other third parties for preclinical research studies and testing, clinical trials and manufacturing services. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice and, as a result, are not included in the table of contractual obligations and commitments above. Payments due upon cancellation consist only of payments for services provided and expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service

providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies and clinical trials; and
- CMOs in connection with the production of preclinical and clinical trial materials.

We base our expenses related to external research and development services on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Revenue Recognition

The terms of our collaboration agreements may include consideration such as non-refundable license fees, funding of research and development services, payments due upon the achievement of clinical and pre-clinical performance-based development milestones, regulatory milestones, manufacturing services, sales-based milestones and royalties on product sales.

We recognize revenue under Accounting Standards Codification 606, or ASC 606, Revenue from Contracts with Customers, which applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. ASC 606 provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of the new revenue standard, we perform the following five steps: (i) identify the promised goods or services in the contract; (ii) determine whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measure the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations; and (v) recognize revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. We then allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled.

We recognize the transaction price allocated to upfront license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from the other performance obligations identified in the contract. If the license is considered to not be distinct from other performance obligations, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied (i) at a point in time, but only for licenses determined to be distinct from other performance obligations in the contract, or (ii) over time; and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from license payments. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

For each collaboration that includes development milestone payments, we evaluate whether it is probable that the consideration associated with each milestone will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until they meet this threshold. Milestones tied to

regulatory approval, and therefore not within our control, are considered constrained until such approval is received. Upfront and ongoing development milestones per our collaboration agreements are not subject to refund if the development activities are not successful. At the end of each subsequent reporting period, we re-evaluate the probability of a significant reversal of the cumulative revenue recognized for the milestones, and, if necessary, adjust the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues from collaborators in the period of adjustment. We exclude sales-based milestone payments and royalties from the transaction price until the sale occurs (or, if later, until the underlying performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied), because the license to our intellectual property is deemed to be the predominant item to which the royalties relate as it is the primary driver of value.

ASC 606 requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in ASC 606 as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which we have sold the same performance obligation separately are not available, we are required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever we determine that a contract should be accounted for as a combined performance obligation we will utilize the cost-to-cost input method. Revenue will be recognized over time using the cost-to-cost input method, based on the total estimated costs to fulfill the obligations. We will recognize revenue as services are being delivered. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement.

We evaluate our collaborative agreements for proper classification in the consolidated statements of operations based on the nature of the underlying activity. Transactions between collaborators recorded in our consolidated statements of operations are recorded on either a gross or net basis, depending on the characteristics of the collaborative relationship.

For revenue generating arrangements where we, as a vendor, provide consideration to a licensor or collaborator, as a customer, we apply the accounting standard that governs such transactions. This standard addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the transaction price unless we receive an identifiable benefit for the payment and we can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of the transaction price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer, and then as an expense. Payments that are not deemed to be a reduction of the transaction price are recorded as an expense.

Consideration that does not meet the requirements to satisfy the above revenue recognition criteria is a contract liability and is recorded as deferred revenue in the consolidated balance sheets. Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with the Sanofi Agreement, we have recorded short-term and long-term deferred revenue on our consolidated balance sheets based on our best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months. Amounts that we expect will not be recognized within the next 12 months are classified as long-term deferred revenue.

The estimate of deferred revenue also reflects management's estimate of the periods of our involvement in certain of our collaborations. Our performance obligations under these collaborations consist of participation on steering committees and the performance of other research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in revenue recognition amounts. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that we will recognize and record in future periods.

Under ASC 606, we will recognize revenue and record a receivable when we fulfill our performance obligations under the Sanofi Agreement. When no further performance obligation is required to be satisfied, we will recognize revenue for the portion satisfied and record a receivable. Amounts are recorded as accounts receivable when our right to consideration is unconditional. A contract liability is recognized when a customer prepays consideration or owes prepayment to an entity according to a contract. We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less or the amount is immaterial.

Business Combinations

We accounted for our acquisition of the MRT Program as a business combination. We account for business combinations using the acquisition method of accounting. Application of this method of accounting requires that (1) identifiable assets acquired (including identifiable intangible assets) and liabilities assumed generally be measured and recognized at fair value as of the acquisition date and (2) the excess of the purchase price over the net fair value of identifiable assets acquired and liabilities assumed be recognized as goodwill, which is not amortized for accounting purposes but is subject to testing for impairment at least annually. Acquired IPR&D is recognized at fair value and initially characterized as an indefinite-lived intangible asset, irrespective of whether the acquired IPR&D has an alternative future use. Transaction costs related to business combinations are expensed as incurred.

Determining the fair value of assets acquired and liabilities assumed in a business combination requires that we use significant judgment and estimates, especially with respect to intangible assets. Critical estimates in valuing certain identifiable assets include, but are not limited to, the selection of valuation methodologies, estimates of future revenue and cash flows, expected long-term market growth, future expected operating expenses, costs of capital and appropriate discount rates. Our estimates of fair value are based upon assumptions we believed to be reasonable, but which are inherently uncertain and, as a result, actual results may differ materially from estimates.

During the measurement period, which extends no later than one year from the acquisition date, we may record certain adjustments to the carrying value of the assets acquired and liabilities assumed with the corresponding offset to goodwill. After the measurement period, all adjustments are recorded in the consolidated statements of operations as operating expenses or income.

Valuation of Contingent Consideration

Contingent consideration reflected on our consolidated balance sheets consists of liabilities for potential milestone and earnout payment obligations and anti-dilution rights recorded in connection with our acquisition of the MRT Program in December 2016. Contingent consideration is initially recognized at fair value at the acquisition date and is subsequently remeasured to fair value at each reporting date, with changes recorded in our consolidated statements of operations. Significant judgment is required in estimating fair value. Our estimates of fair value are based upon assumptions we believed to be reasonable, but which are inherently uncertain and, as a result, actual results may differ materially from estimates.

The fair value of the contingent consideration related to the potential future milestone and earnout payments was estimated by us on the acquisition date and is estimated by us at each reporting date based, in part, on the results of a third-party valuation. The third-party valuation is prepared using a discounted cash flow analysis based on various assumptions, including the probability of achieving specified events, discount rates and the period of time until the earnout payments are payable and the conditions triggering the milestone payments are met.

The fair value of the contingent consideration related to the anti-dilution rights was estimated by us on the acquisition date and was estimated by us at each reporting date based, in part, on the results of a third-party valuation. The third-party valuation was prepared using a probability-weighted expected return method, or PWERM, which considers as inputs the probability of occurrence of events that would trigger the issuance of additional shares, the expected timing of such events, the expected value of the contingently issuable equity upon the occurrence of a triggering event and a risk-adjusted discount rate. As a result of our IPO, we have fully satisfied our obligation to issue shares of common stock to Shire under the Shire Agreement and as a result there is no liability related to the anti-dilution rights as of December 31, 2018.

Impairment of In-Process Research and Development

IPR&D reflected on our consolidated balance sheets consists of indefinite- and definite-lived intangible assets recorded in connection with our acquisition of the MRT Program in December 2016. Indefinite-lived IPR&D is not subject to amortization, but is tested annually for impairment or more frequently if there are indicators of impairment. We test our indefinite-lived IPR&D annually for impairment on October 1st. In testing indefinite-lived IPR&D for impairment, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that its fair value is less than its carrying amount, or we can perform a quantitative impairment analysis to determine the fair value of the indefinite-lived IPR&D without performing a qualitative assessment. Qualitative factors that we consider include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If we choose to first assess qualitative factors and we determine that it is more likely than not that the fair value of the indefinite-lived IPR&D is less than its carrying amount, we would then determine the fair value of the indefinite-lived IPR&D. Under either approach, if the fair value of the indefinite-lived IPR&D is less than its carrying amount, an impairment charge would be recognized for the difference between the fair value and the carrying amount in the consolidated statements of operations. Significant judgment is required in testing IPR&D for impairment, and changes in estimates and assumptions could materially affect the determination of whether impairment exists and, if so, the amount of that impairment.

During the years ended December 31, 2018 and 2017, we did not recognize any impairment charges related to our indefinite-lived IPR&D.

In December 2018, we submitted an IND to the FDA to support the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. In January 2019, the FDA notified us that our IND for MRT5201 was placed on clinical hold. We determined this clinical hold was an indicator of impairment and as a result we retested the indefinite-lived IPR&D asset related to the OTC program for impairment. We performed a quantitative impairment analysis of the indefinite-lived IPR&D related to the OTC program and determined it was not impaired. Therefore, we did not recognize an impairment charge

Impairment of Goodwill

Goodwill reflected on our consolidated balance sheets consists of an intangible asset recorded in connection with our acquisition of the MRT Program in December 2016. Goodwill is not subject to amortization, but is tested annually for impairment or more frequently if there are indicators of impairment. We test our goodwill annually for impairment on October 1st. We have determined that there is a single reporting unit for purposes of testing goodwill for impairment. We have the option to first assess qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that the fair value of the reporting unit was less than its carrying amount, or we can perform a two-step quantitative impairment analysis without performing a qualitative assessment. Examples of such events or circumstances considered in our qualitative assessment include, but are not limited to, a significant adverse change in legal or business climate, an adverse regulatory action or unanticipated competition. If we choose to first assess qualitative factors and we determine that it is more likely than not that the fair value of the reporting unit is less than its carrying amount, we would then perform a two-step quantitative impairment test.

The two-step test starts with comparing the fair value of the reporting unit to the carrying amount of the reporting unit, including goodwill. If the fair value of the reporting unit exceeds the carrying amount, no impairment loss is recognized. However, if the fair value of the reporting unit is less than the carrying value, we must perform the second step of the impairment test to determine if goodwill is impaired. If we determine that goodwill is impaired, the carrying value of the goodwill is written down to its fair value and an impairment charge is recognized in the consolidated statements of operations. Significant judgment is required in testing goodwill for impairment, and changes in estimates and assumptions could materially affect the determination of whether impairment exists and, if so, the amount of that impairment.

During the years ended December 31, 2018 and 2017, we did not recognize any impairment charges related to goodwill.

Stock-Based Compensation

We measure stock-based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards with service-based vesting conditions, we recognize compensation expense using the straight-line method. For stock-based awards with both performance-based and service-based vesting conditions, we recognize compensation expense using the graded-vesting method over the requisite service period, commencing when achievement of the performance condition becomes probable. We recognize adjustments to compensation expense for forfeitures as they occur. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free

interest rate for a period that approximates the expected term of the option, and our expected dividend yield. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date.

Through December 31, 2018, for stock-based awards granted to non-employee consultants, we recognize compensation expense over the period during which services are rendered by such non-employee consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

Determination of the Fair Value of Common Stock

Prior to our IPO, there was no public market for our common stock. The estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation to the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Following the closing of our IPO, the fair value of our common stock is determined based on the quoted market price of our common stock.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K.

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

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15 of Part IV 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.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures" as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports 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. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act 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. In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, who serve as our principal executive officer and principal financial and accounting officer, respectively, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2018.

Management's Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Remediation of Prior Material Weakness in Internal Control Over Financial Reporting

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

We previously identified and disclosed in our Registration Statement on Form S-1 filed with the SEC on June 1, 2018 as well as in our Quarterly Report on Form 10-Q for the periods ended June 30, 2018 and September 30, 2018, a material weakness in our internal control over financial reporting regarding the following:

- we did not design and maintain effective controls and procedures over our accounting for and reporting of the income tax impacts of complex business combinations in fiscal year 2016.

During the second half of 2018, we implemented changes to our process to improve our internal control over financial reporting with respect to the accounting for and reporting of significant transactions, including the tax impacts of complex business transactions. Our management has concluded, based on evidence obtained in validating the design and operating effectiveness of the controls, that the efforts undertaken to enhance the design of our controls over significant transactions, including engaging third-party tax experts when needed and related control activities, which were implemented and executed in 2018, would lead to the prevention or detection of a material misstatement of our consolidated financial statements. As such, our management concluded that we have remediated this material weakness as of December 31, 2018.

Changes in Internal Control over Financial Reporting

There have been no changes in internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the fiscal quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included under the captions "Executive Officers," "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders, which is expected to be filed no later than 120 days after the end of our last fiscal year ended December 31, 2018 and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, including our principal executive, financial and accounting officers, and our directors and employees. We have posted the text of our Code of Business Conduct and Ethics under the "Investors & Media — Corporate Governance" section of our website, *www.translate.bio*. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required by this Item 11 will be included under the captions "Executive and Director Compensation" and "Compensation Committee Interlocks and Insider Participation" in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans" in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included, as applicable, under the captions "Employment Arrangements," "Director Independence" and "Transactions with Related Persons" in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included under the captions "Audit Fees and Services" and "Pre-Approval Policies and Procedures" in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Financial Statements

The following documents are included on pages F-1 through F-40 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

		Incorporation by Reference			
Exhibit Number	**Description**	**Form**	**Date of Filing**	**Exhibit Number**	**Filed Herewith**
2.1+†	Asset Purchase Agreement, by and between the Registrant and Shire Human Genetic Therapies, Inc. dated as of December 22, 2016	S-1^	June 1, 2018	2.1	
3.1	Restated Certificate of Incorporation of Translate Bio, Inc.	8-K^^	July 2, 2018	3.1	
3.2	Amended and Restated Bylaws of Translate Bio, Inc.	8-K^^	July 2, 2018	3.2	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1^	June 1, 2018	4.1	
10.1	Amended and Restated Registration Rights Agreement, by and among the Registrant and the other parties thereto, dated as of December 22, 2016	S-1^	June 1, 2018	10.1	
10.2+	Exclusive Patent License Agreement between the Massachusetts Institute of Technology and Shire AG, dated as of November 1, 2013, as amended	S-1^	June 1, 2018	10.2	
10.3*	Form of Indemnification Agreement with directors and executive officers	S-1^	June 1, 2018	10.3	
10.4*	2016 Stock Incentive Plan, as amended	S-1^	June 1, 2018	10.4	
10.5*	Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan	S-1^	June 1, 2018	10.5	

10.6*	Form of Nonstatutory Stock Option Agreement under the 2016 Stock Incentive Plan	S-1^	June 1, 2018	10.6	
10.7*	2018 Equity Incentive Plan	S-1/A^	June 12, 2018	10.7	
10.8*	Form of Stock Option Agreement under the 2018 Equity Incentive Plan (Single Trigger Acceleration)	S-1^	June 1, 2018	10.8	
10.9*	Form of Stock Option Agreement under the 2018 Equity Incentive Plan (Double Trigger Acceleration)	S-1^	June 1, 2018	10.9	
10.10*	2018 Employee Stock Purchase Plan	S-1^	June 1, 2018	10.10	
10.11*	Letter Agreement, dated October 31, 2014, by and between the Registrant and Ronald C. Renaud, Jr.	S-1^	June 1, 2018	10.11	
10.12*	Letter Agreement, dated August 5, 2016, by and between the Registrant and Thomas G. McCauley, Ph.D.	S-1^	June 1, 2018	10.12	
10.13*	Letter Agreement, dated December 9, 2016, by and between the Registrant and Michael W. Heartlein, Ph.D.	S-1^	June 1, 2018	10.13	
10.14	Lease Agreement, dated June 29, 2017, by and between Translate Bio MA, Inc. and ARE-MA Region No. 8, LLC	S-1^	June 1, 2018	10.14	
10.15*	Consulting Agreement, dated June 1, 2012, as amended, by and between the Registrant and Daniel S. Lynch	S-1^	June 1, 2018	10.15	
10.16*	Consulting Agreement, dated July 1, 2016, by and between the Registrant and Owen Hughes	S-1^	June 1, 2018	10.16	
10.17*	Letter Agreement, dated April 19, 2018, as revised on April 23, 2018, by and between the Registrant and Thomas G. McCauley, Ph.D.	S-1^	June 1, 2018	10.17	
10.18*	Letter Agreement, dated May 14, 2018, by and between the Registrant and John R. Schroer	S-1^	June 1, 2018	10.18	
10.19*	Translate Bio, Inc. Director Compensation Policy	S-1/A^	June 12, 2018	10.19	
10.20+	Collaboration and License Agreement, dated June 8, 2018, by and between Translate Bio MA, Inc. and Sanofi Pasteur Inc.	S-1/A^	June 12, 2018	10.20	
10.21+	First Amendment to Asset Purchase Agreement, by and between the Registrant and Shire Human Genetic Therapies, Inc., dated as of June 7, 2018	S-1/A^	June 12, 2018	10.21	
21.1	List of Subsidiaries	S-1^	June 1, 2018	21.1	
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X

31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X

101.INS XBRL Instance Document
101.SCH XBRL Taxonomy Extension Schema Document
101.CAL XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF XBRL Taxonomy Extension Definition Linkbase Document
101.LAB XBRL Taxonomy Extension Label Linkbase Document
101.PRE XBRL Taxonomy Extension Presentation Linkbase Document
* Indicates management contract or compensatory plan
^ SEC File No. 333-225368
^^ SEC File No. 001-38550

+ Confidential treatment has been requested and/or granted as to certain portions, which portions have been omitted and filed separately with the U.S. Securities and Exchange Commission.
† Pursuant to Item 601(b)(2) of Regulation S-K, the Registrant agrees to furnish supplementally a copy of any omitted schedule or exhibit to the Asset Purchase Agreement to the Securities and Exchange Commission upon request.

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, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Translate Bio, Inc.

Date: March 21, 2019

By: /s/ Ronald C. Renaud, Jr.
Ronald C. Renaud, Jr.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Ronald C. Renaud, Jr. Ronald C. Renaud, Jr.	President and Chief Executive Officer, Director (Principal Executive Officer)	March 21, 2019
/s/ John R. Schroer John R. Schroer	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 21, 2019
/s/ Daniel S. Lynch Daniel S. Lynch	Chairman of the Board	March 21, 2019
/s/ Daniella Beckman Daniella Beckman	Director	March 21, 2019
/s/ Jean-Francois Formela, M.D. Jean-François Formela, M.D.	Director	March 21, 2019
/s/ Brian M. Gallagher, Jr., Ph.D. Brian M. Gallagher, Jr., Ph.D.	Director	March 21, 2019
/s/ Owen Hughes Owen Hughes	Director	March 21, 2019
/s/ Robert Meyer, M.D. Robert Meyer, M.D.	Director	March 21, 2019

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Translate Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Translate Bio, Inc. and its subsidiaries (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations, of comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit), and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses and cash outflows from operations since its inception and has an accumulated deficit, that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 of these consolidated financial statements 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.

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

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 21, 2019

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

TRANSLATE BIO, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 55,199	$ 48,058
Short-term investments	88,904	9,997
Prepaid expenses and other current assets	4,474	3,014
Restricted cash	1,025	1,966
Total current assets	149,602	63,035
Property and equipment, net	10,245	6,778
Goodwill	21,359	21,359
Intangible assets, net	106,445	106,842
Deferred offering costs	—	511
Other assets	—	22
Total assets	$ 287,651	$ 198,547
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 5,168	$ 4,594
Accrued expenses	6,547	5,888
Current portion of contingent consideration	—	1,296
Current portion of deferred revenue	2,572	—
Deferred rent	—	307
Total current liabilities	14,287	12,085
Long-term portion of contingent consideration	103,642	79,713
Deferred revenue, net of current portion	41,841	—
Deferred tax liabilities	481	6,039
Deferred rent, net of current portion	2,105	1,329
Total liabilities	162,356	99,166
Commitments and contingencies (Notes 3, 4 and 14)		
Redeemable convertible preferred stock (Series A, B and C), $0.001 par value; no shares and 145,833,064 shares authorized as of December 31, 2018 and 2017, respectively; no shares and 142,288,292 shares issued and outstanding as of December 31, 2018 and 2017, respectively	—	192,896
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares and no shares authorized as of December 31, 2018 and 2017, respectively; no shares issued and outstanding as of December 31, 2018 and 2017	—	—
Common stock, $0.001 par value; 200,000,000 shares and 236,092,611 shares authorized as of December 31, 2018 and 2017, respectively; 45,139,955 shares and 9,582,791 shares issued and outstanding as of December 31, 2018 and 2017, respectively	45	10
Additional paid-in capital	371,257	55,204
Accumulated deficit	(246,203)	(148,808)
Accumulated other comprehensive income	196	79
Total stockholders' equity (deficit)	125,295	(93,515)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 287,651	$ 198,547

The accompanying notes are an integral part of these consolidated financial statements.

TRANSLATE BIO, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2018	**2017**
Collaboration revenue	$ 1,420	$ —
Operating expenses:		
Research and development	58,024	47,023
General and administrative	22,606	14,311
Change in fair value of contingent consideration	25,020	17,914
Total operating expenses	105,650	79,248
Loss from operations	(104,230)	(79,248)
Other income (expense):		
Interest income	1,323	281
Other income (expense), net	(53)	43
Total other income (expense), net	1,270	324
Loss before benefit from income taxes	(102,960)	(78,924)
Benefit from income taxes	5,565	12,481
Net loss	(97,395)	(66,443)
Accretion of redeemable convertible preferred stock to redemption value	(644)	(719)
Net loss attributable to common stockholders	$ (98,039)	$ (67,162)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.64)	$ (8.66)
Weighted average common shares outstanding—basic and diluted	26,945,508	7,756,180

The accompanying notes are an integral part of these consolidated financial statements.

TRANSLATE BIO, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,	
	2018	2017
Net loss	$ (97,395)	$ (66,443)
Other comprehensive income:		
Unrealized gains on available-for-sale securities, net of tax of $0	117	79
Comprehensive loss	$ (97,278)	$ (66,364)

The accompanying notes are an integral part of these consolidated financial statements.

TRANSLATE BIO, INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Capital	Deficit	Income	(Deficit)
Balances at December 31, 2016	121,085,582	$ 150,277	8,532,723	$ 9	$ 43,766	$ (82,365)	$ —	$ (38,590)
Forfeited restricted common stock	—	—	(100,563)	—	—	—	—	—
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $81	21,202,710	41,900	—	—	—	—	—	—
Issuance of common stock in partial settlement of contingent consideration anti-dilution liability (Note 5)	—	—	1,079,765	1	7,977	—	—	7,978
Issuance of common stock as payment of transaction costs in connection with acquisition of MRT Program (Note 4)	—	—	70,866	—	500	—	—	500
Unrealized gains on available-for-sale securities	—	—	—	—	—	—	79	79
Stock-based compensation expense	—	—	—	—	3,680	—	—	3,680
Accretion of redeemable convertible preferred stock to redemption value	—	719	—	—	(719)	—	—	(719)
Net loss	—	—	—	—	—	(66,443)	—	(66,443)
Balances at December 31, 2017	142,288,292	192,896	9,582,791	10	55,204	(148,808)	79	(93,515)
Accretion of redeemable convertible preferred stock to redemption value	—	644	—	—	(644)	—	—	(644)
Conversion of redeemable convertible preferred stock to common stock	(142,288,292)	(193,540)	25,612,109	26	193,514	—	—	193,540
Issuance of common stock in connection with IPO, net of commisions and offering costs	—	—	9,714,371	9	113,183	—	—	113,192
Issuance of common stock in full settlement of contingent consideration anti-dilution liability (Note 5)	—	—	183,619	—	2,387	—	—	2,387
Issuance of common stock due to the aggregation of fractional shares in connection with the reverse stock split	—	—	52	—	—	—	—	—
Forfeited restricted common stock	—	—	(2,446)	—	2	—	—	2
Exercise of stock options	—	—	49,459	—	278	—	—	278
Stock-based compensation expense	—	—	—	—	7,333	—	—	7,333
Unrealized gains on available-for-sale securities	—	—	—	—	—	—	117	117
Net loss	—	—	—	—	—	(97,395)	—	(97,395)
Balances at December 31, 2018	—	$ —	45,139,955	$ 45	$ 371,257	$ (246,203)	$ 196	$ 125,295

The accompanying notes are an integral part of these consolidated financial statements.

TRANSLATE BIO, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2018	**2017**
Cash flows from operating activities:		
Net loss	$ (97,395)	$ (66,443)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	2,841	1,585
Stock-based compensation expense	7,333	3,680
Change in fair value of contingent consideration	25,020	17,914
Deferred income tax benefit	(5,565)	(12,481)
Accretion of discount on short-term investments	—	(72)
Changes in operating assets and liabilities, net of effects of acquisition:		
Prepaid expenses and other assets	(1,346)	(2,262)
Accounts payable	658	4,025
Accrued expenses	2,271	2,312
Deferred rent	470	954
Deferred revenue	43,580	—
Net cash used in operating activities	(22,133)	(50,788)
Cash flows from investing activities:		
Purchases of investments	(136,694)	(70,767)
Sales and maturities of investments	57,984	73,840
Purchases of property and equipment	(6,580)	(2,769)
Net cash provided by (used in) investing activities	(85,290)	304
Cash flows from financing activities:		
Proceeds from issuance of Series C redeemable convertible preferred stock, net of issuance costs	—	41,900
Proceeds from initial public offering of common stock, net of underwriting discounts and commissions	117,447	—
Payments of initial public offering costs	(4,102)	(153)
Proceeds from option exercises	278	—
Net cash provided by financing activities	113,623	41,747
Net increase (decrease) in cash, cash equivalents and restricted cash	6,200	(8,737)
Cash, cash equivalents and restricted cash at beginning of period	50,024	58,761
Cash, cash equivalents and restricted cash at end of period	$ 56,224	$ 50,024
Cash, cash equivalents and restricted cash at end of period:		
Cash and cash equivalents	$ 55,199	$ 48,058
Restricted cash	1,025	1,966
Total cash, cash equivalents and restricted cash at end of period	$ 56,224	$ 50,024
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ 49	$ 687
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 358
Issuance of common stock in settlement of contingent consideration anti-dilution liability (Note 5)	$ 2,387	$ 7,978
Issuance of common stock as payment of transaction costs in connection with acquisition of MRT Program (Note 4)	$ —	$ 500
Accretion of redeemable convertible preferred stock to redemption value	$ 644	$ 719

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business and Basis of Presentation

Translate Bio, Inc. (the "Company") is a clinical-stage messenger RNA ("mRNA") therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction. Using its proprietary mRNA therapeutic platform ("MRT platform"), the Company creates mRNA that encodes functional proteins. The Company's mRNA is delivered to the target cell where the cell's own machinery recognizes it and translates it, restoring or augmenting protein function to treat or prevent disease. The Company is initially focused on restoring the expression of intracellular and transmembrane proteins, areas that have eluded conventional protein therapeutics, in patients with genetic diseases where there is high unmet medical need.

The Company is developing its lead MRT product candidate for the lung, MRT5005, for the treatment of cystic fibrosis ("CF"). The Company is conducting a Phase 1/2 clinical trial to evaluate the safety and efficacy of MRT5005 and anticipates reporting interim data from this trial in the second half of 2019. The Company is developing its lead MRT product candidate for the liver, MRT5201, for the treatment of ornithine transcarbamylase ("OTC") deficiency. In December 2018, the Company submitted an investigational new drug application ("IND") for MRT5201, which the U.S. Food and Drug Administration (the "FDA") has placed on clinical hold. The FDA is requiring additional preclinical toxicology data. The Company has identified the additional preclinical studies required, and plans to complete these studies and submit a response to the FDA in the fourth quarter of 2019.

In December 2016, the Company acquired from Shire Human Genetic Therapies, Inc. ("Shire"), a subsidiary of Shire plc, rights to the assets of Shire's mRNA therapy platform (the "MRT Program"), including the cystic fibrosis transmembrane conductance regulator ("CFTR") and OTC deficiency mRNA therapy programs. In connection with this acquisition, Shire received shares of the Company's common stock, with related anti-dilution rights, and is eligible for future milestone and earnout payments on products developed with the MRT technology (see Note 4).

The Company is subject to risks common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and include the accounts of the Company and its wholly owned subsidiaries, Translate Bio MA, Inc. and Translate Bio Securities Corporation, from their date of incorporation. All intercompany accounts and transactions have been eliminated in consolidation.

Reverse Stock Split

On June 15, 2018, the Company effected a one-for-5.5555 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's redeemable convertible preferred stock (see Note 8). 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 reverse stock split and the associated adjustment of the preferred stock conversion ratios.

Initial Public Offering

On June 27, 2018, the Company's registration statement on Form S-1 relating to its initial public offering of its common stock ("the IPO") was declared effective by the Securities and Exchange Commission ("SEC"). In the IPO, which closed on July 2, 2018, the Company issued and sold 9,350,000 shares of common stock at a public offering price of $13.00 per share. On July 24, 2018, the Company issued and sold an additional 364,371 shares of common stock at a price of $13.00 per share pursuant to the exercise of the underwriters' over-allotment option in the IPO. The aggregate net proceeds to the Company from the IPO, inclusive of the proceeds from the over-allotment exercise, were $113.2 million after deducting underwriting discounts and commissions of $8.8 million and offering expenses of $4.3 million. Upon closing of the IPO, all 142,288,292 shares of the Company's redeemable convertible preferred stock then outstanding converted into an aggregate of 25,612,109 shares of common stock.

Sanofi Pasteur Collaboration and Licensing Agreement

On June 8, 2018, the Company entered into a collaboration and license agreement with Sanofi Pasteur Inc. ("Sanofi"), the vaccines global business unit of Sanofi S.A., to develop mRNA vaccines for up to five infectious disease pathogens (the "Sanofi Agreement"). The Sanofi Agreement became effective on July 9, 2018. Under the Sanofi Agreement, the Company and Sanofi will jointly conduct research and development activities to advance mRNA vaccines and mRNA vaccine platform development during a three-year research term, which may be extended by mutual agreement. Following the research term, the Company is obligated to manufacture clinical product for Sanofi, which the Company estimates may take up to eight years to complete.

The Company is eligible to receive up to $805.0 million in payments, which includes an upfront payment of $45.0 million, which the Company received in July 2018; certain development, regulatory and sales-related milestones across several vaccine targets; and option exercise fees if Sanofi exercises its option related to development of vaccines for additional pathogens. The Company is also eligible to receive tiered royalty payments associated with worldwide sales of the developed vaccines, if any (see Note 3).

Going Concern

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through December 31, 2018, the Company has funded its operations with proceeds from the sale of redeemable convertible preferred stock and the sale of bridge units, which ultimately converted into shares of preferred stock, the proceeds from the IPO and an upfront payment received under the Sanofi Agreement. The Company has incurred recurring losses and cash outflows from operations since its inception, including net losses of $97.4 million and $66.4 million for the years ended December 31, 2018 and 2017, respectively. In addition, the Company had an accumulated deficit of $246.2 million as of December 31, 2018.

The Company expects to continue to generate operating losses for the foreseeable future. As of March 21, 2019, the date of issuance of these consolidated financial statements, the Company expects that its cash, cash equivalents and short-term investments of $144.1 million as of December 31, 2018 will be sufficient to fund its operating expenses and capital expenditure requirements into the second quarter of 2020. The Company expects to seek additional funding through equity financings, debt financings, or other capital sources, including collaborations with other companies or other strategic transactions. Although management continues to pursue these plans to fund continuing operations, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company, if at all.

If the Company is unable to obtain funding, the Company will be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations.

Based on its recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance its future operations, the Company concluded that there was substantial doubt about its ability to continue as a going concern.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, the revenue recognized from collaboration agreements, the valuation of common stock and stock-based awards, the valuation of assets acquired and liabilities assumed in business combinations, and the impairment of identifiable intangible assets and goodwill. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Cash and Cash Equivalents

All highly liquid investments purchased with an original maturity date of three months or less at the date of purchase are considered to be cash equivalents. Cash equivalents consisted of money market funds as of December 31, 2018 and 2017.

Investments

The Company's debt security investments are classified as available-for-sale and are carried at fair value, with the unrealized gains and losses reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses and declines in value determined to be other than temporary are based on the specific identification method and are included as a component of other income (expense), net in the consolidated statements of operations.

The Company evaluates its investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the statement of operations. No such adjustments were necessary during the periods presented.

The Company's investments as of December 31, 2018 and 2017 had original maturities of less than one year.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents as well as short-term investments. Cash, cash equivalents and short-term investments consist of demand deposits, money market funds and U.S. government agency bonds. The Company generally maintains balances in various operating accounts with financial institutions that management believes to be of high credit quality, in amounts that may exceed federally insured limits. The Company has not experienced any losses related to its cash, cash equivalents and short-term investments and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Restricted Cash

In connection with its operating lease commitments, the Company issued letters of credit collateralized by cash deposits that are classified as restricted cash in the consolidated balance sheets. Restricted cash amounts have been classified as current assets based on the release dates of the restrictions under the letters of credit, which occur annually.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations. As of December 31, 2018, the Company had no deferred offering costs. As of December 31, 2017, the Company recorded deferred offering costs of $0.5 million in connection with its IPO.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful lives of each asset. Estimated useful lives are periodically assessed to determine if changes are appropriate. Upon retirement or sale, the related cost and accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in the consolidated statements of operations. Repair and maintenance costs are expensed as incurred. The estimated useful lives of the Company's property and equipment are as follows:

	Estimated Useful Life
Laboratory equipment	5 years
Computer equipment	3 years
Office equipment	5 years
Leasehold improvements	Shorter of lease term or 10 years

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated or amortized in accordance with the above useful lives once placed into service.

Property and equipment are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate an asset group for recoverability, the Company compares the forecasted undiscounted cash flows expected to result from the use and eventual disposition of the asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use and eventual disposition of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows using market participant assumptions. The Company did not record any impairment losses on property and equipment during the years ended December 31, 2018 and 2017.

Revenue Recognition

The terms of the Company's collaboration agreements may include consideration such as non-refundable license fees, funding of research and development services, payments due upon the achievement of clinical and pre-clinical performance-based development milestones, regulatory milestones, manufacturing services, sales-based milestones and royalties on product sales.

The Company had no revenue prior to the Sanofi Agreement, therefore the adoption of Financial Accounting Standards Board ("FASB") ASC 606, *Revenue from Contracts with Customers*, ("ASC 606"), described further in Note 3 under the heading "Accounting under ASC 606", had no impact to the Company. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance contracts, financial instruments, guarantees and nonmonetary exchanges. ASC 606 provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the promised goods or services in the contract; (ii) determine whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measure the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations; and (v) recognize revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when collectability of the consideration to which the Company is entitled in exchange for the goods or services the Company transfers to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. The Company then allocates the transaction price (the amount of consideration the Company expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled and will not result in a significant reversal of revenue when the uncertainty with the variable consideration is resolved.

The Company recognizes the transaction price allocated to upfront license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from

the other performance obligations identified in the contract. If the license is considered to not be distinct from other performance obligations, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied (i) at a point in time, but only for licenses determined to be distinct from other performance obligations in the contract, or (ii) over time, and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from license payments. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Sanofi Agreement entitles the Company to additional payments upon the achievement of performance-based milestones. These milestones are generally categorized into three types: development milestones, generally based on the advancement of the Company's pipeline and initiation of clinical trials; regulatory milestones, generally based on the submission, filing or approval of regulatory applications such as a new drug application ("NDA") in the United States; and sales-based milestones, generally based on meeting specific thresholds of sales in certain geographic areas. The Company is also eligible to receive from Sanofi tiered royalty payments on worldwide net sales of mRNA vaccines. For each collaboration that includes development milestone payments, the Company evaluates whether it is probable that the consideration associated with each milestone will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until they meet this threshold. Milestones tied to regulatory approval, and therefore not within the Company's control, are considered constrained until such approval is received. Upfront and ongoing development milestones per its collaboration agreements are not subject to refund if the development activities are not successful. At the end of each subsequent reporting period, the Company re-evaluates the probability of a significant reversal of the cumulative revenue recognized for the milestones, and, if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues from collaborators in the period of adjustment. The Company may enter into an agreement that includes sales-based milestone payments and royalties in exchange for a license of intellectual property. The Company considers the underlying facts and circumstances of these agreements, noting whether the future payments are contingent upon future sales and whether they are dependent on a third party's ability to successfully commercialize a product using the licensed intellectual property. The Company also considers whether the license is the only, or predominant, item to which the milestone payments and royalties relate. If the Company concludes the license is the predominant item in the agreement, therefore the primary driver of value, the Company excludes sales-based milestone payments and royalties from the transaction price until the sale occurs (or, if later, until the underlying performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied). Currently, the Company has not recognized any royalty revenue resulting from the Sanofi Agreement.

ASC 606 requires the Company to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in ASC 606 as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which the Company has sold the same performance obligation separately are not available, the Company is required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever the Company determines that a contract should be accounted for as a combined performance obligation it will utilize the cost-to-cost input method. Revenue will be recognized over time using the cost-to-cost input method, based on the total estimated costs to fulfill the obligations. The Company will recognize revenue as services are delivered. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement.

The Company evaluates its collaborative agreements for proper classification in the consolidated statements of operations based on the nature of the underlying activity. Transactions between collaborators recorded in the Company's consolidated statements of operations are recorded on either a gross or net basis, depending on the characteristics of the collaborative relationship.

For revenue generating arrangements where the Company, as a vendor, provides consideration to a licensor or collaborator, as a customer, the Company applies the accounting standard that governs such transactions. This standard addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the transaction price unless the Company receives an identifiable benefit for the payment and it can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of the transaction price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer, and then as an expense. Payments that are not deemed to be a reduction of the transaction price are recorded as an expense.

Consideration that does not meet the requirements to satisfy the above revenue recognition criteria is a contract liability and is recorded as deferred revenue in the consolidated balance sheets. Although the Company follows detailed guidelines in measuring revenue, certain judgments affect the application of its revenue policy. For example, in connection with the Sanofi Agreement, the Company has recorded short-term and long-term deferred revenue on its consolidated balance sheets based on the Company's best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months. Amounts that the Company expects will not be recognized within the next 12 months are classified as long-term deferred revenue.

The estimate of deferred revenue also reflects management's estimate of the periods of the Company's involvement in certain of its collaborations. The Company's performance obligations under these collaborations consist of participation on steering committees and the performance of other research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, the Company's estimates may change in the future. Such changes to estimates would result in a change in revenue recognition amounts. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that the Company will recognize and record in future periods. At December 31, 2018, the Company had short-term and long-term deferred revenue of $2.6 million and $41.8 million, respectively, related to the Sanofi Agreement.

Under ASC 606, the Company will recognize revenue and record a receivable when it fulfills its performance obligations under the Sanofi Agreement. When no further performance obligation is required to be satisfied, the Company will recognize revenue for the portion satisfied and record a receivable. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less or the amount is immaterial. At December 31, 2018, the Company has not capitalized any costs to obtain any of its contracts.

Business Combinations

The Company accounts for business combinations using the acquisition method of accounting. Application of this method of accounting requires that (i) identifiable assets acquired (including identifiable intangible assets) and liabilities assumed generally be measured and recognized at fair value as of the acquisition date and (ii) the excess of the purchase price over the net fair value of identifiable assets acquired and liabilities assumed be recognized as goodwill, which is not amortized for accounting purposes but is subject to testing for impairment at least annually. Acquired in-process research and development ("IPR&D") is recognized at fair value and initially characterized as an indefinite-lived intangible asset, irrespective of whether the acquired IPR&D has an alternative future use. Transaction costs related to business combinations are expensed as incurred.

Determining the fair value of assets acquired and liabilities assumed in a business combination requires management to use significant judgment and estimates, especially with respect to intangible assets. Critical estimates in valuing certain identifiable assets include, but are not limited to, the selection of valuation methodologies, estimates of future revenue and cash flows, expected long-term market growth, future expected operating expenses, costs of capital and appropriate discount rates. Management's estimates of fair value are based upon assumptions believed to be reasonable, but which are inherently uncertain and, as a result, actual results may differ materially from estimates.

During the measurement period, which extends no later than one year from the acquisition date, the Company may record certain adjustments to the carrying value of the assets acquired and liabilities assumed with the corresponding offset to goodwill. After the measurement period, all adjustments are recorded in the consolidated statements of operations as operating expenses or income.

Acquisition-related contingent consideration, which consists of potential milestone and earnout payment obligations as well as anti-dilution rights provided to Shire (see Note 3), was recorded in the consolidated balance sheets at its acquisition-date estimated fair value, in accordance with the acquisition method of accounting. The fair value of the acquisition-related contingent consideration is remeasured each reporting period, with changes in fair value recorded in the consolidated statements of operations. The fair value measurement is based on significant inputs not observable by market participants and thus represents a Level 3 input in the fair value hierarchy (see Note 4).

Asset Acquisitions

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire IPR&D with no alternative future use is charged to expense at the acquisition date.

In-Process Research and Development

The fair value of IPR&D acquired through a business combination is capitalized as an indefinite- and definite-lived intangible asset until the completion or abandonment of the related research and development activities. When the related research and development is completed or a change in circumstance occurs that defines the useful life, the asset is reclassified to a definite-lived asset and amortized over its estimated useful life. When a change between these classes occurs, the Company will perform an impairment test.

The fair value of an IPR&D intangible asset is typically determined using an income approach whereby management forecasts the net cash flows expected to be generated by the asset over its estimated useful life. The net cash flows reflect the asset's stage of completion, the probability of technical success, the projected costs to complete, expected market competition, and an assessment of the asset's life-cycle. The net cash flows are then adjusted to present value by applying an appropriate discount rate that reflects the risk factors associated with the cash flow streams.

Indefinite-lived IPR&D is not subject to amortization, but is tested annually for impairment or more frequently if there are indicators of impairment. The Company tests its indefinite-lived IPR&D annually for impairment on October 1st. In testing indefinite-lived IPR&D for impairment, the Company has the option to first assess qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that its fair value is less than its carrying amount, or the Company can perform a quantitative impairment analysis to determine the fair value of the indefinite-lived IPR&D without performing a qualitative assessment. Qualitative factors that the Company considers include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If the Company chooses to first assess qualitative factors and the Company determines that it is more likely than not that the fair value of the indefinite-lived IPR&D is less than its carrying amount, the Company would then determine the fair value of the indefinite-lived IPR&D. Under either approach, if the fair value of the indefinite-lived IPR&D is less than its carrying amount, an impairment charge is recognized in the consolidated statements of operations. During the years ended December 31, 2018 and 2017, the Company did not recognize any impairment charges related to its definite-lived IPR&D (see Note 4).

In December 2018, the Company submitted an IND to the FDA to support the initiation of a Phase 1/2 clinical trial for MRT5201 in patients with OTC deficiency. In January 2019, the FDA notified the Company that its IND for MRT5201 was placed on clinical hold. The Company determined this clinical hold was an indicator of impairment and as a result, retested the indefinite-lived IPR&D related to the OTC program for impairment. The Company performed a quantitative impairment analysis whereby the Company forecasted the net cash flows expected to be generated by the indefinite-lived IPR&D related to the OTC program over its estimated useful life. The net cash flows reflected the program's stage of completion, the probability of technical success, the projected costs to complete, expected market competition and an assessment of the program's life-cycle. The net cash flows were then adjusted to present value by applying an appropriate discount rate that reflects the risk factors associated with the cash flow streams. Following this retest the Company determined the indefinite-lived IPR&D related to the OTC program was not impaired. Therefore, the Company did not recognize an impairment charge.

Definite-lived IPR&D is recorded at fair value and amortized over the greater of economic consumption or on a straight-line basis over its estimated useful life. Definite-lived IPR&D is tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If an impairment review is performed to evaluate an asset group for recoverability, the Company compares the forecasted undiscounted cash flows expected to result from the use and eventual disposition of the asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use and eventual disposition of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows using market participant assumptions.

Goodwill

Goodwill represents the excess of the fair value of the consideration transferred over the fair value of the net tangible and identifiable intangible assets acquired in a business combination. Goodwill is not subject to amortization, but is tested annually for impairment or more frequently if there are indicators of impairment. The Company tests its goodwill annually for impairment on October 1st.

The Company has determined that there is a single reporting unit for purposes of testing goodwill for impairment. In testing goodwill for impairment, the Company has the option to first assess qualitative factors to determine whether the existence of events or circumstances would indicate that it is more likely than not that the fair value of the reporting unit was less than its carrying amount, or the Company can perform a two-step quantitative impairment analysis without performing a qualitative assessment. Examples of such events or circumstances considered in the Company's qualitative assessment include, but are not limited to, a significant adverse change in legal or business climate, an adverse regulatory action or unanticipated competition. If the Company chooses to first assess qualitative factors and the Company determines that it is more likely than not that the fair value of its reporting unit is less than its carrying amount, the Company would then perform a two-step quantitative impairment test. The two-step test starts with comparing the fair value of the reporting unit to the carrying amount of a reporting unit, including goodwill. If the fair value of the reporting unit exceeds the carrying amount, no impairment loss is recognized. However, if the fair value of the reporting unit is less than its carrying value, the second step of the impairment test is performed to determine if goodwill is impaired. If the Company determines that goodwill is impaired, the carrying value of the goodwill is written down to its fair value and an impairment charge is recognized in the consolidated statements of operations. During the years ended December 31, 2018 and 2017, the Company did not recognize any impairment charges related to goodwill.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents and short-term investments are carried at fair value, determined based on Level 2 inputs in the fair value hierarchy described above (see Note 5). The Company's contingent consideration liability is carried at fair value, determined based on Level 3 inputs in the fair value hierarchy described above (see Note 5). The carrying values of the Company's prepaid expenses and other current assets, accounts payable, accrued expenses and other short-term liabilities approximate their fair values due to the short-term nature of these assets and liabilities.

Segment Information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company's primary focus is on the advancement of the Company's MRT platform to treat diseases caused by protein or gene dysfunction.

Research and Development Costs

Costs associated with internal research and development and external research and development services, including drug development and preclinical studies, are expensed as incurred. Research and development expenses include costs for salaries, employee benefits, subcontractors, facility-related expenses, depreciation and amortization, including amortization related to definite-lived IPR&D intangible assets, stock-based compensation, third-party license fees, laboratory supplies, and external costs of outside vendors engaged to conduct discovery, preclinical and clinical development activities and clinical trials as well as to manufacture clinical trial materials, and other costs. The Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such prepaid expenses are recognized as an expense when the services have been performed or the goods have been delivered, or when it is no longer expected that the goods will be delivered or the services rendered.

Upfront payments, milestone payments (other than those deemed contingent consideration in a business combination) and annual maintenance fees under license agreements are expensed in the period in which they are incurred.

Research and Development Contract Costs and Accruals

The Company has entered into various research and development-related contracts with companies both inside and outside of the United States. The related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ materially from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-Based Compensation

The Company measures all stock-based awards granted to employees and directors based on their fair value on the date of the grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards with service-based vesting conditions, the Company recognizes compensation expense using the straight-line method. For stock-based awards with both performance-based and service-based vesting conditions, the Company recognizes compensation expense using the graded-vesting method over the requisite service period, commencing when achievement of the performance condition becomes probable. The Company recognizes adjustments to compensation expense for forfeitures as they occur. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and the Company's expected dividend yield (see Note 11). The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of the Company's common stock on that same date.

Through December 31, 2018, for stock-based awards granted to non-employee consultants, compensation expense is recognized over the period during which services are rendered by such non-employee consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

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

Classification and Accretion of Redeemable Convertible Preferred Stock

The Company has classified its redeemable convertible preferred stock outside of stockholders' equity (deficit) because the shares contain certain redemption features that are not solely within the control of the Company. Costs incurred in connection with the issuance of each series of redeemable convertible preferred stock are recorded as a reduction of gross proceeds from issuance. The carrying values of redeemable convertible preferred stock are accreted to their redemption values through a charge to additional paid-

in capital or accumulated deficit over the period from date of issuance to the earliest date on which the holders could, at their option, elect to redeem their shares. Upon the closing of the Company's IPO in July 2018, all then-outstanding shares of Redeemable Convertible Preferred Stock converted into shares of common stock according to their terms. As of December 31, 2018 there were no shares of Redeemable Convertible Preferred Stock authorized, issued or outstanding.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) was unrealized gains (losses) on U.S. government agency bonds, which are classified as available-for-sale-securities.

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 consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year 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 the 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.

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 recognize in the consolidated 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 Income (Loss) per Share

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting net income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period, including potential dilutive shares of common stock. For purposes of this calculation, outstanding stock options, unvested restricted common stock and redeemable convertible preferred stock are considered potential dilutive shares of common stock.

The Company's preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive shares of common stock are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2018 and 2017.

Recently Adopted Accounting Pronouncements

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments (Topic 230)* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented in the statement of cash flows. The adoption of ASU 2016-15 is required to be applied retrospectively. The Company adopted ASU 2016-15 as of the required effective date of January 1, 2018, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230)* ("ASU 2016-18"), which requires that amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted ASU 2016-18 as of the required effective date of January 1, 2018. The effect of the adoption was that the amount of cash and cash equivalents previously presented on the consolidated statements of cash flows for the year ended December 31, 2017 increased by $2.0 million to reflect the inclusion of restricted cash. Additionally, as a result of the adoption, transfers between restricted and unrestricted cash are no longer presented as a component of the Company's investing activities.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation: Scope of Modification Accounting (Topic 718)* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The Company adopted ASU 2017-09 as of the required effective date of January 1, 2018, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02*, Leases (Topic 842)* ("ASU 2016-02"). ASU 2016-02 requires lessees to recognize most leases on their balance sheet as a right-of-use asset and a lease liability. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The guidance is effective for public entities for annual periods beginning after December 15, 2018 and for interim periods within those fiscal years. The Company will adopt ASU 2016-02 effective as of January 1, 2019. In July 2018, the FASB subsequently issued ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements* ("ASU 2018-11"), which includes certain amendments to ASU 2016-02 intended to provide relief in implementing the new standard. Among these amendments is the option to not restate comparative periods presented in the financial statements. The Company has elected this transition approach, using a cumulative-effect adjustment on the effective date of the standard, with comparative periods presented in accordance with the existing guidance in ASC 840. The Company adopted the standard on January 1, 2019 and has used the effective date as its date of initial application. The Company expects to take advantage of certain available expedients by electing the transition package of practical expedients permitted within ASU 2016-02, which allows the Company to not reassess previous accounting conclusions around whether arrangements are, or contain, leases, the classification of leases, and the treatment of initial direct costs. The Company also has made an accounting policy election to exclude leases with an initial term of twelve months or less from the balance sheet.

The Company is still assessing the impact of adopting the new standard, and currently expects a material impact to its consolidated balance sheet in recognizing additional lease liabilities and right-of-use assets as of January 1, 2019 related to its operating leases. The Company further expects to provide enhanced new disclosures about its leasing arrangements in its financial statements for future periods. The Company does not expect that the new standard will have a material impact on the Company's consolidated statement of operations or cash flows.

In June 2016, the FASB issued guidance on the Measurement of Credit Losses on Financial Instruments. The guidance requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, the standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. This standard will be effective for the Company on January 1, 2020. The Company is currently evaluating the potential impact that this standard may have on the Company's consolidated financial statements and related disclosures.

In January 2017, the FASB issued ASU No. 2017-04, *Intangibles—Goodwill and Other: Simplifying the Test for Goodwill Impairment (Topic 350)* ("ASU 2017-04"), which provides for the elimination of Step 2 from the goodwill impairment test. If impairment charges are recognized, the amount recorded will be the amount by which the carrying amount exceeds the reporting unit's fair value with certain limitations. ASU 2017-04 is effective for fiscal years beginning after December 15, 2019. The Company does not expect that the adoption of this new standard will have a material impact on its consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718)* ("ASU 2018-07"), which aligns the accounting for share-based payment awards issued to employees and non-employees. Under the new guidance, the existing employee guidance will apply to non-employee share-based transactions. The new guidance is effective on January 1, 2019. The Company does not expect that the adoption of this new standard will have a material impact on its consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*. This new standard modifies certain disclosure requirements on fair value measurements. This new standard will be effective on January 1, 2020. Early adoption, of the entire amendments or on the provisions that eliminate or modify the requirements, is permitted. The Company does not expect that the adoption of this new standard will have a material impact on its disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808)* ("ASU 2018-18"). This update provides clarification on the interaction between *Revenue Recognition* (Topic 606) and *Collaborative Arrangements* (Topic 808) including the alignment of unit of account guidance between the two topics. This update is effective in fiscal years, including interim periods, beginning after December 15, 2020, and early adoption is permitted. The Company is currently evaluating the impact on its consolidated financial statements of adopting this guidance.

3. Collaboration Agreement

Sanofi Collaboration and License Agreement

On June 8, 2018, the Company entered into the Sanofi Agreement, a collaboration and license agreement with Sanofi to develop mRNA vaccines and mRNA vaccine platform development for up to five infectious disease pathogens (the "Licensed Fields"). The Sanofi Agreement became effective on July 9, 2018.

Under the Sanofi Agreement, the Company and Sanofi have agreed to collaborate to perform certain research and development activities to advance mRNA vaccines and mRNA vaccine platform development during a three-year research term, which may be extended by mutual agreement. Following the research term, the Company is obligated to manufacture clinical product for Sanofi, which the Company estimates may take up to eight years to complete. The collaboration activities will be subject to a collaboration plan to be updated annually. The Sanofi Agreement provides for Sanofi to make an upfront payment to the Company of $45.0 million, which the Company received in July 2018, as well as certain potential milestone payments and option payments, each as further described below. In addition, the Company is eligible to receive from Sanofi tiered royalty payments on worldwide net sales of mRNA vaccines.

Under the Sanofi Agreement, the Company and Sanofi created a governance structure, including committees and working groups, to manage the activities under the collaboration. If the Company and Sanofi do not mutually agree on certain decisions, Sanofi would be able to break a deadlock without the Company's consent. The collaboration includes an estimated budget. Sanofi is responsible for paying the Company's employee costs, out-of-pocket costs paid to third parties and manufacturing costs, up to a specified amount.

Under the terms of the Sanofi Agreement, the Company has granted to Sanofi exclusive, worldwide licenses under applicable patents, patent applications, know-how and materials, including those arising under the collaboration, to develop, commercialize and manufacture mRNA vaccines to prevent, treat or cure diseases, disorders or conditions in humans caused by any of three of the Licensed Fields. In addition, pursuant to the terms of the Sanofi Agreement and subject to certain limitations, Sanofi has options to add up to two additional infectious disease pathogens within the granted licenses to the Licensed Fields by exercising either option or both options during a specified option term and paying the Company a $5.0 million fee per added pathogen. If, prior to the exercise of the options by Sanofi, the Company receives a bona fide third-party offer to acquire rights to the field to which an option relates, the Company must notify Sanofi of such offer, and if Sanofi does not exercise its option as to the applicable field, such field will no longer be subject to the option.

The Company and Sanofi retain the rights to perform their respective obligations and exercise their respective rights under the Sanofi Agreement, and Sanofi may grant sublicenses to affiliates or third parties. Sanofi has also granted the Company non-exclusive, sublicensable licenses under patent rights claiming certain improvements that Sanofi may make to the technology the Company has licensed to it or claiming certain technology arising from the collaboration and owned by Sanofi. The Company may exercise such licenses to develop, manufacture and commercialize products, other than products that use a vaccine to prevent, treat or cure a disease, disorder or condition in humans caused by an infectious disease pathogen. If the Company commercializes any product covered by such a Sanofi patent right, the Company would pay Sanofi a royalty of a low single-digit percentage. Sanofi may terminate these licenses to the Company if the Company materially breaches the terms of the license and the breach remains uncured for a specified period, which may be extended in certain circumstances.

Sanofi has sole responsibility for all commercialization activities for mRNA vaccines in the Licensed Fields and is obligated to bear all costs in connection with any such commercialization. The Company and Sanofi intend to enter into a supply agreement pursuant to which the Company would be responsible for manufacturing certain non-clinical and clinical mRNA vaccines and materials containing mRNA until the Company transfers such manufacturing capabilities to Sanofi. The Company would be entitled to receive payments for manufacturing mRNA vaccines under the supply agreement.

The Sanofi Agreement provides that the Company is eligible to receive aggregate potential payments of up to $805.0 million from Sanofi, which includes an upfront payment, potential milestone payments and potential option exercise payments. In July 2018, Sanofi paid the Company a $45.0 million upfront payment in respect of the licenses and options granted to Sanofi. Sanofi will also pay the Company $5.0 million with respect to each additional Licensed Field for which it exercises an option. Sanofi has also agreed to pay the Company milestone payments upon the achievement of specified development, regulatory and commercialization milestones. In particular, the Company is entitled to receive development and regulatory milestone payments of up to $63.0 million per Licensed Field and sales milestone payments of up to $85.0 million per Licensed Field. In addition, the Company is entitled to receive a $10.0 million milestone payment from Sanofi following completion of the technology and process transfer.

Sanofi has agreed to pay the Company a tiered royalty on worldwide net sales of all mRNA vaccines within each Licensed Field ranging from a high single-digit percentage to a low teens percentage, depending on quarterly net sales by Sanofi, its affiliates and its sublicensees. The royalty paid to the Company can be reduced with respect to a product once the relevant licensed patent rights expire or if additional licensed technology is required, but the royalty payments generally may not fall below the Company's royalty obligations to third parties plus a royalty of a low single-digit percentage. Royalty payments under the Sanofi Agreement are payable on a product-by-product and country-by-country basis beginning on the launch of the product in the country until the later of the expiration of the last valid claim covering such product or 10 years after the launch of such product in such country.

The Sanofi Agreement provides that it will remain in effect until terminated in accordance with its terms. Either the Company or Sanofi may terminate the Sanofi Agreement in its entirety if the other party is subject to certain insolvency proceedings. Either party may terminate the Sanofi Agreement in its entirety or with respect to a particular Licensed Field, country or product if the other party materially breaches the Sanofi Agreement and the breach remains uncured for a specified period, which may be extended in certain circumstances. Sanofi may also terminate the Sanofi Agreement in its entirety or with respect to a particular Licensed Field, country or product for safety reasons or for convenience, in each case after a specified notice period. After termination of the Sanofi Agreement, Sanofi may continue to manufacture and commercialize the terminated products for a specified period of time, subject to Sanofi's payment obligations.

Accounting Under ASC 606

In determining the appropriate amount of revenue to be recognized under ASC 606, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined 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.

The Company identified the following promised goods or services contained in the Sanofi Agreement: (i) the license it conveyed to Sanofi with respect to the Licensed Fields, (ii) the licensed know-how to be conveyed to Sanofi with respect to the Licensed Fields, (iii) it obligations to perform research and development on the Licensed Fields, (iv) its obligation to transfer licensed materials to Sanofi, (v) its obligation to manufacture and supply certain non-clinical and clinical mRNA vaccines and materials containing mRNA until the Company transfers such manufacturing capabilities to Sanofi and (vi) the technology and process transfer. The Company assessed whether each of these promised goods or services are distinct performance obligations on their own or if they need to be combined with other promises to create a bundle that is a distinct performance obligation. The Company determined that the promised goods and services do not have standalone value and are highly interrelated. Accordingly, the promised goods and

services represent one performance obligation. Sanofi's right to exercise options for up to two additional infectious disease pathogens within the granted licenses to the Licensed Fields are accounted for separately as they do not represent material rights, based on the criteria of ASC 606. Upon the exercise of any option by Sanofi, the contract promises associated with an option target would use a separate proportional performance model for purposes of revenue recognition under ASC 606.

The Company determined the transaction price of the Sanofi Agreement to be $161.1 million based upon the probability that the consideration associated with each milestone or reimbursement will not be subject to a significant reversal in the cumulative amount of revenue recognized. The transaction price includes the upfront, non-refundable payment of $45.0 million for the transfer of the combined license, supply and development obligations under the Sanofi Agreement, an estimated $32.6 million in reimbursable employee costs, an estimated $54.5 million in reimbursable development costs including out-of-pocket costs paid to third parties and manufacturing costs, an estimated $19.0 million in milestone payments and an estimated $10.0 million for scaling up the Company's manufacturing capacity. Reimbursable development costs are payable by Sanofi within 60 days of invoicing. There was no significant financing component or noncash consideration included in the Sanofi Agreement.

Under ASC 606, the Company recognized revenue using the cost-to-cost input method, which it believes best depicts the transfer of control to the customer. Under the cost-to-cost input method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified performance obligation. Under this method, revenue is recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. The estimate of the Company's measure of progress and estimate of variable consideration to be included in the transaction price will be updated at each reporting date as a change in estimate. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time.

The following table summarizes the Company's net revenues from collaboration (in thousands):

	Year Ended December 31,	
	2018	2017
Collaboration revenue	$ 1,420	$ —

The following table presents the balance of the Company's contract liabilities (in thousands):

	December 31,	
	2018	2017
Contract liabilities		
Deferred revenues	$ 44,413	$ —

The Company has accounts receivable of $0.8 million from Sanofi, which is included in prepaids and other current assets on the consolidated balance sheet as of December 31, 2018.

The Company considers the total consideration expected to be earned in the next 12 months for services to be performed as short-term deferred revenue, and consideration that is expected to be earned subsequent to 12 months from the balance sheet date as long-term deferred revenue. The Company expects to complete its obligations and recognize all net revenues from the collaboration over eight years.

4. Acquisitions, Goodwill and Other Intangible Assets

Acquisition of Shire's MRT Program

On December 22, 2016, the Company entered into an asset purchase agreement (as amended on June 7, 2018, the "Shire Agreement") with Shire pursuant to which Shire sold equipment to and assigned to the Company all of its rights to certain patent rights, permits, real property leases, contracts, regulatory documentation, books and records, and materials related to Shire's MRT Program, including its CFTR and OTC deficiency mRNA therapeutic programs. The Company assumed no liabilities of Shire as part of the Shire Agreement. As part of the acquisition, the scientific founders of the MRT platform and other key members of the Shire program joined the Company to advance the Company's MRT platform and the development of its product candidates. Under the Shire Agreement, the Company is obligated to use commercially reasonable efforts to develop and seek and obtain regulatory approval for products that include or are composed of MRT compounds covered by or derived from patent rights or know-how acquired from Shire ("MRT Products") and to achieve specific developmental milestones. During the earnout period described below, with respect to any MRT Product in any country, the Company is obligated to use commercially reasonable efforts to market and sell such MRT Product in such country.

The Company accounted for the acquisition of the assets and employees as a business combination. As consideration for the acquisition, the Company issued 5,815,560 shares of common stock to Shire and agreed to make potential future milestone and earnout payments to Shire upon the occurrence of specified commercial milestones. In particular, the Company is obligated to make milestone payments to Shire of up to $60.0 million in the aggregate upon the occurrence of specified commercial milestones, including upon the first commercial sale of an MRT Product for the treatment of CF and upon the achievement of a specified level of annual net sales with respect to an MRT Product. The Company is also obligated to make additional milestone payments of $10.0 million for each non-CF MRT Product upon the first commercial sale of a non-CF MRT Product; provided that such milestone payments will only be due once for any two non-CF MRT Products that contain the same MRT compounds or once per non-CF MRT Product that is a vaccine developed under the Company's collaboration with Sanofi (see Note 3).

Under the Shire Agreement, the Company is also obligated to pay a quarterly earnout payment of a mid-single-digit percentage of net sales of each MRT Product. The earnout period, which is determined on a product-by-product and country-by-country basis, will begin on the date of the first commercial sale of such MRT Product in such country and will end on the later of (i) 10 years after such first commercial sale and (ii) the expiration of the last valid claim of the patent rights acquired from Shire or derived from patent rights or know-how acquired from Shire covering such MRT Product in such country.

Under the Shire Agreement, the Company was obligated to consummate an equity financing of at least $100.0 million (the "Subsequent Financing"). As part of the Shire Agreement, the Company provided Shire anti-dilution rights whereby it agreed to issue Shire additional common stock such that Shire would own, upon the completion of the Subsequent Financing, either (i) 18.0% of the Company's common stock on an as-converted and fully diluted basis or (ii) if less, 19.9% of the voting power of all then outstanding common stock of the Company, excluding shares of unvested restricted stock. As a result of the Company's IPO, the Company fully satisfied the Subsequent Financing obligation. In addition, as a result of and concurrent with the closing of the Company's IPO on July 2, 2018, the Company issued 183,619 shares of common stock to Shire in full satisfaction of the Company's anti-dilution obligations to Shire (see Note 5).

Elements of Purchase Consideration

As part of its accounting for the business combination, the Company recorded the fair value of the common stock issued on the acquisition date as well as contingent consideration liabilities for the potential future milestone and earnout payments and for the anti-dilution rights provided to Shire through the completion of the Subsequent Financing. The aggregate acquisition-date fair value of consideration transferred was determined to be $112.2 million, consisting of the following (in thousands):

Fair value of common stock	$	41,089
Fair value of contingent consideration — potential milestone and earnout payments		62,666
Fair value of contingent consideration — anti-dilution rights		8,407
Total fair value of purchase consideration	$	112,162

Common Stock Issued at Closing. The fair value of the 5,815,560 shares of common stock issued on the acquisition date, aggregating $41.1 million, was determined based on the fair value of $7.06 per share of common stock estimated by the Company at the acquisition date based, in part, on the results of a third-party valuation. The third-party valuation was prepared using a hybrid method, which used market approaches to estimate the Company's equity value, including an OPM backsolve based on the $1.98 price per share of Series C redeemable convertible preferred stock sold by the Company in a Series C financing on the same date as the acquisition date of the MRT Program (see Note 8). The hybrid method is a probability-weighted expected return method ("PWERM") where the equity value in one or more of the scenarios is allocated using an option-pricing method ("OPM"). In the third-party valuation, two types of future-event scenarios were considered: an IPO scenario and a remain-private scenario. Each type of future-event scenario was probability weighted by the Company based on an evaluation of its historical and forecasted performance and operating results, an analysis of market conditions at the time, and its expectations as to the timing and likely prospects of the future-event scenarios. A discount for lack of marketability was then applied to arrive at an indication of fair value per share of the common stock.

Liabilities for Contingent Consideration. The fair value of the contingent consideration related to potential future milestone and earnout payments that may be due to Shire was estimated by the Company at the acquisition date based, in part, on the results of a third-party valuation. The third-party valuation was prepared using a discounted cash flow analysis based on various assumptions, including the probability of achieving specified events, discount rates, and the period of time until earnout payments are payable and the conditions triggering the milestone payments are met.

The fair value of the contingent consideration related to Shire's anti-dilution rights was estimated by the Company at the acquisition date based, in part, on the results of a third-party valuation. The third-party valuation was prepared using a PWERM,

which considered as inputs the probability of occurrence of events that would trigger the issuance of additional shares, the expected timing of such events, the expected value of the contingently issuable equity upon the occurrence of a triggering event and a risk-adjusted discount rate.

The Company assessed the anti-dilution rights provided to Shire and determined that the rights (i) met the definition of a freestanding financial instrument that was not indexed to the Company's own stock and (ii) did not meet the definition of a derivative. As the rights did not meet the definition of a derivative and did not qualify for equity classification, the Company determined to classify the anti-dilution rights as a liability. Accordingly, the Company recognized the liability at fair value on the acquisition date and recognizes changes in the fair value of the anti-dilution rights at each subsequent reporting period in the consolidated statements of operations (see Note 5).

Allocation of the Purchase Consideration

The acquisition of Shire's MRT Program was accounted for in accordance with the acquisition method of accounting for business combinations. Acquisition-related costs totaling $3.0 million were expensed to general and administrative expenses as incurred. Such acquisition-related costs included $0.5 million for the services of the investment bank that facilitated the acquisition payable in shares of the Company's common stock, which was satisfied in December 2017 through the Company's issuance of 70,866 shares of common stock. The total consideration transferred was allocated to the tangible and identifiable intangible assets acquired based on their estimated fair values as follows (in thousands):

Identifiable intangible assets	$	106,907
Property and equipment		2,416
Deferred tax assets		1,308
Deferred tax liabilities		(18,520)
Valuation allowance for deferred tax assets		(1,308)
Goodwill		21,359
Total purchase price consideration	$	112,162

Identifiable intangible assets acquired in the acquisition consisted of IPR&D and a lease-based asset. The IPR&D included ongoing projects that could further the Company's preclinical and clinical development activities related to CF, OTC and other potential rare diseases. The lease-based intangible asset related to the below-market rental expense that the Company was expected to benefit from over the remaining lease period at one of its leased facilities. The IPR&D was determined to be indefinite-lived, and the lease-based intangible asset was determined to be definite-lived, with an estimated useful life of 1.5 years. The fair values of the identifiable intangible assets as of the acquisition date were as follows (in thousands):

In-process research and development — MRT	$	45,992
In-process research and development — CF		42,291
In-process research and development — OTC		18,559
Lease agreement		65
Total identifiable intangible assets	$	106,907

The fair value of the IPR&D assets acquired was estimated by the Company at the acquisition date based, in part, on the results of the third-party valuation. The third-party valuation was prepared using the multi-period excess earnings method ("MPEEM"), a form of the income approach, which assumes the fair value of an intangible asset is equal to the present value of the incremental risk-adjusted after-tax cash flows attributable only to each IPR&D intangible asset. The MPEEM determined the after-tax cash flows, adjusted for contributory charges and cumulative probabilities of technical success. The probability-adjusted cash flows were then discounted to present value by the selected discount rate and added to the tax amortization benefit to determine the fair value. The key assumptions used in this model were net revenue projections, phase of development assumptions and discount rates. Upon commencement of the Sanofi Agreement, the IPR&D - MRT intangible asset was reclassified from indefinite-lived to definite-lived intangible assets and the Company began amortization of this intangible asset. Amortization will be recorded over an estimated eight-year period based on an economic consumption model. For the year ended December 31, 2018, the Company recorded amortization expense of $0.4 million related to the definite-lived IPR&D - MRT intangible asset. The estimated aggregate amortization expense for each of the five succeeding fiscal years is $3.2 million, $9.7 million, $10.5 million, $5.3 million and $2.0 million for the years ended December 31, 2019, 2020, 2021, 2022 and 2023, respectively.

A deferred tax liability of $18.5 million was recorded as part of the business combination for the non-deductible portion of the indefinite-lived IPR&D acquired. As part of the business combination, the Company also recorded $1.3 million of acquired deferred

tax assets related to depreciation of property and equipment, but recorded those with a full valuation allowance due to the uncertainty of realizing a benefit from those assets.

The excess of the fair value of the consideration transferred over the fair value of identifiable assets acquired in the acquisition was allocated to goodwill in the amount of $21.4 million. Goodwill resulting from the acquisition was allocated to the Company's single reporting unit and was largely attributed to the synergies and economies of scale expected from combining the research and operations of the MRT Program and the Company. Substantially all of the goodwill recorded as part of the MRT Program acquisition is not deductible for U.S. federal income tax purposes.

The results of operations of the MRT Program business have been included in the Company's consolidated statements of operations from the acquisition date. The operations of the MRT Program business were fully integrated into the Company's operations and no separate financial results of the business were maintained.

On June 7, 2018, the Company and Shire entered into an amendment to the Shire Agreement to align certain terms of the Shire Agreement with the collaboration and license agreement that the Company entered into with Sanofi on June 8, 2018. Pursuant to this amendment, an mRNA vaccine that is developed pursuant to the Company's collaboration with Sanofi will be considered an MRT Product if it includes an MRT compound having an mRNA sequence that encodes a protein that is from, or that binds to, an infectious disease pathogen in a field that has been licensed by the Company to Sanofi. Pursuant to the amended Shire Agreement, the Company is obligated to make milestone payments of $10.0 million for each non-CF MRT Product upon the first commercial sale of a non-CF MRT Product; provided that such milestone payments will only be due once for any two non-CF MRT Products that contain the same MRT compounds or once per non-CF MRT Product that is a vaccine developed under the Company's collaboration with Sanofi. The Company has concluded that this amendment will not affect the contingent purchase consideration recorded for accounting purposes.

5. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	Fair Value Measurements as of December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ —	$ 23,318	$ —	$ 23,318
U.S. government agency bonds	—	88,904	—	88,904
	$ —	$ 112,222	$ —	$ 112,222
Liabilities:				
Contingent consideration	$ —	$ —	$ 103,642	$ 103,642
	$ —	$ —	$ 103,642	$ 103,642

	Fair Value Measurements as of December 31, 2017 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ —	$ 28,636	$ —	$ 28,636
U.S. government agency bonds	—	9,997	—	9,997
	$ —	$ 38,633	$ —	$ 38,633
Liabilities:				
Contingent consideration	$ —	$ —	$ 81,009	$ 81,009
	$ —	$ —	$ 81,009	$ 81,009

During the years ended December 31, 2018 and 2017, there were no transfers between Level 1, Level 2 and Level 3.

Cash equivalents as of December 31, 2018 and 2017 consisted of money market funds totaling $23.3 million and $28.6 million, respectively. The money market funds were valued using inputs observable in active markets for similar securities, which represent a Level 2 measurement in the fair value hierarchy. The Company's short-term investments as of December 31, 2018 and 2017 consisted of U.S. government agency bonds and were classified as available-for-sale securities. The U.S. government agency bonds were valued using inputs observable in active markets for similar securities, which represent a Level 2 measurement in the fair value hierarchy. As

of December 31, 2018, the Company's short-term investments had an amortized cost of $88.7 million, an unrealized loss of $0.2 million and a fair value of $88.9 million. All of these securities have a maturity of one year or less.

Valuation of Contingent Consideration

The contingent consideration liability related to the acquisition of the MRT Program was classified as Level 3 measurement within the fair value hierarchy and includes the potential future milestone and earnout payments that may be due by the Company to Shire (see Note 4) and prior to the IPO, an anti-dilution liability with respect to shares issuable by the Company to Shire upon a qualified financing event (see Note 4).

The fair value of the liability to make potential future milestone and earnout payments was estimated by the Company at each reporting date based, in part, on the results of a third-party valuation using a discounted cash flow analysis based on various assumptions, including the probability of achieving specified events, discount rates, and the period of time until earnout payments are payable and the conditions triggering the milestone payments are met. The actual settlement of contingent consideration could differ from current estimates based on the actual occurrence of these specified events.

The fair value of the anti-dilution liability was estimated by the Company at each reporting date based, in part, on the results of a third-party valuation using the PWERM, which considers as inputs the probability of occurrence of events that would trigger the issuance of shares, the expected timing of such events, the expected value of the contingently issuable equity upon the occurrence of a triggering event and a risk-adjusted discount rate.

The following tables presents the unobservable inputs and fair value of the components of the contingent consideration (dollar amounts in thousands):

	Unobservable Inputs at December 31, 2018 and 2017		Fair Value at December 31,	
	Discount Rate	Projected Year of Payment	2018	2017
Earnout payments	14.5% - 15.0%	2025 - 2039	$ 94,999	$ 72,896
Milestone payments	14.5% - 15.0%	2025 - 2030	8,643	6,817
Anti-dilution rights	1.39% - 1.64%	N/A	—	1,296
			$ 103,642	$ 81,009

The following table presents a roll-forward of the total acquisition-related contingent consideration liability (in thousands):

	Fair Value
Balance as of December 31, 2017	$ 81,009
Change in fair value of contingent consideration	25,020
Issuance of common stock in full settlement of contingent consideration anti-dilution liability	(2,387)
Balance as of December 31, 2018	$ 103,642

The increase in the fair value of contingent consideration during the year ended December 31, 2018 was primarily due to the continued progress of MRT5005, including the initiation in May 2018 of the Company's Phase 1/2 clinical trial of MRT5005 for the treatment of patients with CF, the continued advancement of MRT5201 for the treatment of patients with OTC deficiency, the IND for which has been placed on clinical hold by the FDA, the time value of money due to the passage of time, as well as a decrease in the discount rate.

In December 2017, as a result of the Company's issuance and sale of 21,202,710 shares of Series C redeemable convertible preferred stock at that same time (see Note 8), the Company issued to Shire 1,079,765 shares of common stock, with an aggregate fair value of $8.0 million, pursuant to the anti-dilution rights conveyed to Shire in the Shire Agreement (see Note 4). The shares issued to Shire were in partial settlement of the Company's anti-dilution contingent consideration liability that was recorded in its purchase accounting for the MRT Program in December 2016 and reflected as current portion of contingent consideration on the Company's consolidated balance sheet as of December 31, 2017. The Company's obligation related to these anti-dilution rights remained in effect until the Company consummated an additional equity financing of $7.0 million. After giving effect to the closing of the Company's IPO, which satisfied the Subsequent Financing requirement (see Note 4), the Company issued an additional 183,619 shares of common stock to Shire in full satisfaction of the Company's anti-dilution obligations to Shire.

6. Property and Equipment, Net

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

	December 31,	
	2018	2017
Laboratory equipment	$ 7,012	$ 5,382
Computer equipment	686	481
Office equipment	836	249
Leasehold improvements	5,635	1,131
Construction in progress	959	2,591
	15,128	9,834
Less: Accumulated depreciation and amortization	(4,883)	(3,056)
	$ 10,245	$ 6,778

Depreciation and amortization expense related to property and equipment was $2.4 million and $1.5 million for the years ended December 31, 2018 and 2017, respectively. Construction in progress recorded as of December 31, 2017 primarily related to in-process construction of leasehold improvements, which were transferred to leasehold improvements in April 2018 upon completion.

7. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued employee compensation and benefits	$ 2,933	$ 2,252
Accrued external research and development expenses	1,901	1,115
Accrued consultant and professional fees	977	1,130
Other	736	1,391
	$ 6,547	$ 5,888

8. Redeemable Convertible Preferred Stock

As of December 31, 2018 and 2017, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue no shares and 145,833,064 shares, respectively, of redeemable convertible preferred stock. As of December 31, 2017, the Company had 36,194,026 shares of Series A redeemable convertible preferred stock (the "Series A preferred stock"), 59,133,987 shares of Series B redeemable convertible preferred stock (the "Series B preferred stock") and 46,960,279 shares of Series C redeemable convertible preferred stock (the "Series C preferred stock") issued and outstanding. The Series A preferred stock, Series B preferred stock and Series C preferred stock were redeemable and convertible by the holders under specified conditions. The redeemable convertible preferred stock is classified outside of stockholders' equity (deficit) because the shares contained redemption features that are not solely within the control of the Company. The Series A preferred stock, Series B preferred stock and Series C preferred stock are collectively referred to as the "Redeemable Convertible Preferred Stock."

In December 2017, the Company issued and sold 21,202,710 shares of Series C preferred stock at a price of $1.98 per share for aggregate proceeds of $41.9 million, net of issuance costs of $0.1 million.

Upon issuance of each class of Redeemable Convertible Preferred Stock, the Company assessed the embedded conversion and liquidation features of the securities and determined that such features did not require the Company to separately account for these features. The Company also concluded that no beneficial conversion feature existed upon the issuance date of each class of Redeemable Convertible Preferred Stock or as of December 31, 2017.

Upon the closing of the Company's IPO on July 2, 2018, all then-outstanding shares of Redeemable Convertible Preferred Stock converted into an aggregate of 25,612,109 shares of common stock according to their terms. As of December 31, 2018, there were no shares of Redeemable Convertible Preferred Stock authorized, issued or outstanding.

As of December 31, 2017, Redeemable Convertible Preferred Stock consisted of the following (in thousands, except share amounts):

	December 31, 2017				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	36,194,026	36,194,026	$ 36,194	$ 36,194	6,514,986
Series B preferred stock	59,133,987	59,133,987	64,002	63,199	10,644,210
Series C preferred stock	50,505,051	46,960,279	92,700	92,981	8,452,913
	145,833,064	142,288,292	$ 192,896	$ 192,374	25,612,109

The holders of the Redeemable Convertible Preferred Stock had the following rights and preferences prior to the conversion on Preferred Stock into common stock upon the completion of the Company's IPO:

Voting

The holders of Redeemable Convertible Preferred Stock were entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote and had the right to vote the number of shares equal to the number of shares of common stock into which each share of Redeemable Convertible Preferred Stock could convert on the record date for determination of stockholders entitled to vote. In addition, the holders of Series A preferred stock were entitled to elect two directors of the Company, and the holders of Series B preferred stock were entitled to elect one director of the Company.

Conversion

Each share of Redeemable Convertible Preferred Stock was convertible, at the option of the holder, at any time after the date of issuance. In addition, each share of Redeemable Convertible Preferred Stock would be automatically converted into shares of common stock at the applicable conversion ratio then in effect (i) upon the closing of a firm-commitment public offering resulting in at least $50.0 million of gross proceeds to the Company at a price of at least $13.20 per share of common stock, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization, or (ii) upon the written consent of the holders of at least 60% of the then-outstanding shares of Redeemable Convertible Preferred Stock, voting together as a single class.

The conversion ratio of each series of Redeemable Convertible Preferred Stock was determined by dividing the Original Issue Price of each series by the Conversion Price of each series. The Original Issue Price per share was $1.00 for Series A preferred stock, $1.0593 for Series B-1 preferred stock, $1.00 for Series B-2 preferred stock, $1.0305 for Series B-3 preferred stock, $1.0330 for Series B-4 preferred stock, $1.0381 for Series B-5 preferred stock, $1.0513 for Series B-6 preferred stock, $1.0426 for Series B-7 preferred stock, $1.08 for Series B-8 preferred stock and $1.98 for Series C preferred stock. The Series B-1, Series B-2, Series B-3, Series B-4, Series B-5, Series B-6, Series B-7 and Series B-8 preferred stock are referred to collectively as "Series B preferred stock."

Upon completion of the Company's IPO, each share of each series of Redeemable Convertible Preferred Stock was convertible into shares of common stock on a 5.5555-for-one basis. The Conversion Price per shares at issuance was $5.5555 for Series A preferred stock, $5.8849 for Series B-1 preferred stock, $5.5555 for Series B-2 preferred stock, $5.7249 for Series B-3 preferred stock, $5.7388 for Series B-4 preferred stock, $5.7672 for Series B-5 preferred stock, $5.8405 for Series B-6 preferred stock, $5.7922 for Series B-7 preferred stock, $5.9999 for Series B-8 preferred stock and $10.9999 for Series C preferred stock, each subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization and other adjustments as set forth in the Company's certificate of incorporation, as amended and restated.

Dividends

The holders of the Redeemable Convertible Preferred Stock were entitled to receive noncumulative dividends when, as and if declared by the board of directors. The Company could not pay any dividends on shares of common stock of the Company unless the holders of Redeemable Convertible Preferred Stock then outstanding simultaneously receive dividends at the same rate and same time as dividends are paid with respect to common stock. Through December 31, 2018 and 2017, no cash dividends have been declared or paid.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event (as defined below), the holders of the then-outstanding Redeemable Convertible Preferred Stock were entitled to receive, in preference to any distributions to the common stockholders, an amount per share equal to the Original Issue Price per share of each

respective share of Redeemable Convertible Preferred Stock, plus all dividends declared but unpaid on such shares. In the event that the assets available for distribution to the Company's stockholders were not sufficient to permit payment to the holders of Redeemable Convertible Preferred Stock in the full amount to which they were entitled, the assets available for distribution would be distributed on a pro rata basis among the holders of the Redeemable Convertible Preferred Stock in proportion to the respective amounts otherwise payable in respect of the shares of Redeemable Convertible Preferred Stock. After the payments were made in full to the holders of Redeemable Convertible Preferred Stock, to the extent available, the remaining amounts would be distributed among the holders of the Redeemable Convertible Preferred Stock and common stock, pro rata based on the number of shares held by each holder.

Unless the holders of at least 60% of the then-outstanding Redeemable Convertible Preferred Stock, voting together as a single class, elected otherwise, a Deemed Liquidation Event would include a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

Redemption

At the written election of at least 60% of the holders of Redeemable Convertible Preferred Stock, voting together as a single class, the shares of Redeemable Convertible Preferred Stock outstanding were redeemable, at any time on or after December 22, 2021, in three equal annual installments commencing no more than 60 days after written notice, in an amount equal to the Original Issue Price per share of each series of Redeemable Convertible Preferred Stock plus all declared but unpaid dividends thereon.

9. Preferred Stock

On July 2, 2018, in connection with the closing of the Company's IPO, the Company filed its restated certificate of incorporation, which authorizes the Company to issue up to 10,000,000 shares of preferred stock, $0.001 par value per share. There are no shares of preferred stock outstanding as of December 31, 2018.

10. Common Stock

As of December 31, 2017, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 236,092,611 shares of common stock, $0.001 par value per share. On July 2, 2018, the Company filed it restated certificate of incorporation, which authorizes the Company to issue up to 200,000,000 shares of common stock, $0.001 par value per share.

Each share of common stock entitles the holder to one vote for each share of common stock held. Common stockholders are entitled to receive dividends, as declared by the board of directors. These dividends are subject to the preferential dividend rights of the holders of the Company's preferred stock. Through December 31, 2018 and 2017, no cash dividends have been declared or paid.

As of December 31, 2017, the Company had reserved 32,115,490 shares of common stock for the conversion of outstanding shares of Redeemable Convertible Preferred Stock (see Note 9), the exercise of outstanding stock options (see Note 11) and the number of shares remaining available for future issuance under the 2016 Stock Incentive Plan (see Note 11). Upon completion of the Company's IPO on July 2, 2018, all shares of Redeemable Convertible Preferred Stock converted to common stock.

11. Incentive Stock Options and Restricted Stock

2018 Equity Incentive Plan

On March 7, 2018, the Company's board of directors, subject to stockholder approval, adopted, and on June 15, 2018, its stockholders approved, the 2018 Equity Incentive Plan (the "2018 Plan"), which became effective on June 27, 2018. The 2018 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards.

The number of shares initially reserved for issuance under the 2018 Plan is the sum of 2,512,187, plus the number of shares (up to 1,013,167 shares) equal to the sum of (i) the number of shares remaining available for issuance under the 2016 Stock Incentive Plan, as amended, (the "2016 Plan"), upon the effectiveness of the 2018 Plan, which was 360,514 shares, and (ii) the number of shares of common stock subject to outstanding awards under the 2016 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares of common stock that may be issued under the 2018 Plan will automatically increase on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2019 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2028, equal to the lowest of (i) 3,349,582 shares, (ii) 4% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. The shares of common stock underlying any awards that are

forfeited, canceled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased or are otherwise terminated by the Company under the 2018 Plan will be added back to the shares of common stock available for issuance under the 2018 Plan. During the year ended December 31, 2018, option awards to purchase 203,176 shares of common stock were granted under the 2018 Plan.

Shares that are expired, terminated, surrendered or canceled under the 2018 Plan without having been exercised will be available for future grants of awards. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for the grant of awards.

The 2018 Plan is administered by the board of directors. The exercise prices, vesting periods and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of options may not be less than 100% of the fair market value of the common stock on the date of grant. Stock options awarded under the 2018 Plan expire 10 years after the grant date, unless the board of directors sets a shorter term. Awards granted to employees, officers, members of the board of directors and consultants typically vest over a four-year period.

Unvested stock options are forfeited upon the recipient ceasing to provide services to the Company.

2018 Employee Stock Purchase Plan

On March 7, 2018, the Company's board of directors, subject to stockholder approval, adopted, and on June 15, 2018, its stockholders approved the 2018 Employee Stock Purchase Plan (the "2018 ESPP"), which became effective on June 27, 2018. A total of 418,697 shares of common stock were initially reserved for issuance under this plan. The number of shares of common stock that may be issued under the 2018 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2019 and continuing for each fiscal year until, and including, the fiscal year commencing on January 1, 2029, equal to the lowest of (i) 837,395 shares, (ii) 1% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors.

As of December 31, 2018, no shares had been issued under the 2018 ESPP.

2016 Stock Incentive Plan

The 2016 Plan provided for the Company to issue equity awards to employees, officers and directors, consultants and advisors. Under the 2016 Plan, the Company was allowed to grant stock options, stock appreciation rights, restricted stock and restricted stock units. Shares that are expired, terminated, surrendered or canceled under the 2016 Plan without having been exercised will be available for future grants of awards under the 2018 Plan. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for the grant of awards under the 2018 Plan.

The 2016 Plan was administered by the board of directors. The exercise prices, vesting periods and other restrictions were determined at the discretion of the board of directors, except that the exercise price per share of options may not be less than 100% of the fair market value of the common stock on the date of grant. Stock options awarded under the 2016 Plan expire 10 years after the grant date, unless the board of directors set a shorter term. Stock options and restricted stock granted to employees, officers, members of the board of directors and consultants typically vest over a four-year period.

Upon the effectiveness of the 2018 Plan on June 27, 2018, no further awards will be made under the 2016 Plan. Awards outstanding under the 2016 Plan will continue to be governed by their existing terms. During the year ended December 31, 2018, option awards to purchase 1,966,114 shares of common stock were granted under the 2016 Plan.

Stock Options

The following table summarizes the Company's stock option activity since December 31, 2017 (in thousands, except share and per share amounts):

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Intrinsic Value
Outstanding as of December 31, 2017	4,364,916	$ 7.17	9.79	$ 977
Granted	2,169,290	$ 8.82		
Exercised	(49,459)	$ 5.62		
Forfeited	(248,741)	$ 6.62		
Outstanding as of December 31, 2018	6,236,006	$ 7.78	8.74	$ 1,104
Vested as of December 31, 2018	1,827,004	$ 7.16	7.95	$ 632
Vested and expected to vest as of December 31, 2018	6,236,006	$ 7.78	8.74	$ 1,104
Vested as of December 31, 2017	661,593	$ 7.04	9.72	$ 231
Vested and expected to vest as of December 31, 2017	4,364,916	$ 7.17	9.79	$ 977

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2018 was $0.1 million. There were no options exercised during the year ended December 31, 2017.

The weighted average grant-date fair value per share of stock options granted was $5.95 and $4.10 during the years ended December 31, 2018 and 2017, respectively.

The total fair value of options vested during the years ended December 31, 2018 and 2017 was $4.9 million and $2.6 million, respectively.

Stock Option Valuation

The fair value of stock option grants is estimated using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted to employees and directors:

	Year Ended December 31,	
	2018	2017
Risk-free interest rate	2.81%	2.15%
Expected term (in years)	6.0	6.0
Expected volatility	75.5%	59.0%
Expected dividend yield	0%	0%

The following table presents the assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted to a non-employee:

	Year Ended December 31, 2017
Risk-free interest rate	2.08%
Expected term (in years)	10.0
Expected volatility	60.9%
Expected dividend yield	0%

During the year ended December 31, 2018, the Company did not grant options to non-employees.

Restricted Common Stock

The following table summarizes the Company's restricted stock activity since December 31, 2017:

	Number of Shares	Weighted Average Grant-Date Fair Value
Unvested restricted common stock outstanding as of December 31, 2017	526,478	$ 1.14
Forfeited restricted common stock	(2,446)	$ 1.28
Vested restricted common stock	(304,884)	$ 1.04
Unvested restricted common stock outstanding as of December 31, 2018	219,148	$ 1.27

The total fair value of restricted common stock vested during the years ended December 31, 2018 and 2017 was $0.3 million and $0.4 million, respectively, which the Company recorded as stock-based compensation during those periods.

Stock-Based Compensation

Stock-based compensation expense was classified in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Research and development expenses	$ 3,756	$ 1,886
General and administrative expenses	3,577	1,794
	$ 7,333	$ 3,680

Included in research and development stock-based compensation expense for the year ended December 31, 2018 was $0.3 million related to the modification of options in connection with the resignation of the Company's former Chief Scientific Officer ("CSO"). In connection with this resignation, the Company entered into a separation agreement with the former CSO. Under the terms of the separation agreement, vesting of options for the purchase of 72,871 shares of common stock held by the former CSO was accelerated with no change to the exercise price of such options. Stock options for the purchase of 204,353 shares of common stock, representing all of the options held by the former CSO as of the date of his resignation, are exercisable for one year following his resignation.

As of December 31, 2018, total unrecognized compensation cost related to the unvested stock-based awards was $19.6 million, which is expected to be recognized over weighted average periods of 2.6 years.

12. Income Taxes

On December 22, 2017, the Tax Cuts and Jobs Act (the "Tax Act") was signed into United States law. The Tax Act includes a number of changes to existing tax law, including, among other things, a permanent reduction in the top marginal federal corporate income tax rate from 35% to a flat rate of 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks. The enactment of the Tax Act resulted in the Company recording a net income tax benefit of $6.1 million in the year ended December 31, 2017. The $6.1 million net income tax benefit consisted of (i) the remeasurement of the deferred tax liabilities for the Company's indefinite-lived intangible assets due to the tax rate reduction, which resulted in a corresponding income tax benefit of $3.7 million, and (ii) a reduction in the valuation allowance for deferred tax assets related to deductible temporary differences that will generate unlimited net operating loss carryforwards when they reverse in future periods, which resulted in a corresponding income tax benefit of $2.4 million. No adjustments to the provisional amounts recorded as of December 31, 2017 were recorded during the year ended December 31, 2018.

During 2017, the Company recorded tax charges for the impact of the Tax Act effects using the current available information and technical guidance on the interpretations of the Tax Act. As permitted by SEC Staff Accounting Bulletin 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act, the Company recorded provisional estimates and have subsequently finalized our accounting analysis based on the guidance, interpretations and data available as of December 31, 2018 with no material changes to our estimates.

Income Taxes

During the year ended December 31, 2018, the Company recognized an income tax benefit of $5.6 million, which resulted from a reduction in the deferred tax liabilities recorded as part of the Company's acquisition of the MRT Program. The reduction in the deferred tax liabilities during the year ended December 31, 2018 resulted from an increase in the tax basis of the indefinite-lived IPR&D recorded in the acquisition.

During the year ended December 31, 2017, the Company recognized an income tax benefit of $12.5 million, consisting of (i) a $6.4 million benefit due to a reduction of the same amount in the deferred tax liabilities recorded as part of the Company's acquisition of the MRT Program (see Note 4) and (ii) a $6.1 million benefit resulting from the impact of the Tax Act. The reduction in the deferred tax liabilities during the year ended December 31, 2017 resulted from an increase in 2017 in the tax basis of the indefinite-lived IPR&D recorded in the acquisition.

All of the Company's operating losses since inception have been generated in the United States.

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

	Year Ended December 31,	
	2018	2017
U.S. federal statutory income tax rate	(21.0)%	(34.0)%
State income taxes, net of federal benefit	(6.9)	(5.4)
Research and development tax credits and orphan drug credit	(5.5)	(4.2)
Stock-based compensation	0.5	1.5
Other permanent differences	0.3	0.4
Remeasurement of deferred taxes due to the Tax Act	—	15.9
Change in deferred tax asset valuation allowance	27.7	10.0
Other	(0.4)	—
Effective income tax rate	(5.3)%	(15.8)%

Components of the Company's deferred tax assets and liabilities were as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 50,917	$ 32,524
Research and development tax credit and orphan drug credit carryforwards	13,581	6,372
Depreciation and amortization	2,380	2,025
Accrued expenses and other	2,894	1,090
Total deferred tax assets	69,772	42,011
Deferred tax liabilities:		
Indefinite-lived intangible assets	(2,109)	(8,445)
Total deferred tax liabilities	(2,109)	(8,445)
Valuation allowance	(68,143)	(39,605)
Net deferred tax liabilities	$ (480)	$ (6,039)

As of December 31, 2018, the Company had federal net operating loss carryforwards of $190.8 million, of which $122.1 million will, if not utilized, begin to expire in 2031, and state net operating loss carryforwards of $171.7 million, which will, if not utilized, begin to expire in 2031. As of December 31, 2018, the Company had federal and state research and development tax credits carryforwards of $5.1 million and $2.0 million, respectively, which will, if not utilized, begin to expire in 2032 and 2028, respectively, and orphan drug tax credit carryforwards of $6.6 million, which will, if not utilized, begin to expire in 2037. The Company also has state investment tax credit carryforwards of $0.4 million, which will, if not utilized, begin to expire in 2019.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since inception due to the significant complexity and cost associated with such a study. If the Company has experienced an ownership change, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation on the use of net operating loss carryforwards is known, no amounts are being presented as an uncertain tax position.

In addition, the Company has not conducted a study of its research and development tax credit carryforwards. This study may result in an adjustment to the Company's research and development tax credit carryforwards. Until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize all of the benefits of the deferred tax assets. As of December 31, 2017, a full valuation allowance had been established against the deferred tax assets with the exception of $2.4 million of deferred tax assets related to deductible temporary differences that will generate unlimited net operating loss carryforwards when they reverse in future periods. At December 31, 2018, the Company maintained a full valuation allowance with the exception of $0.8 million related primarily to indefinite-lived net operating loss carryforwards. Management reevaluates the positive and negative evidence at each reporting period.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018 and 2017 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards in 2018 and 2017, and the impact of the Tax Act in 2017, and were as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Valuation allowance at beginning of year	$ (39,605)	$ (31,729)
Decreases recorded as benefit to income tax provision	—	18,628
Increases recorded to income tax provision	(28,538)	(26,504)
Valuation allowance at end of year	$ (68,143)	$ (39,605)

In the year ended December 31, 2018, the increase in the valuation allowance of $28.5 million was driven primarily by the generation of federal and state net operating loss and tax credit carryforwards.

In the year ended December 31, 2017, the decrease in the valuation allowance of $18.6 million consisted of (i) a $16.2 million decrease to offset the corresponding decrease in deferred tax assets remeasured at the lower federal income tax rate and (ii) a $2.4 million decrease due to deductible temporary differences that will generate unlimited net operating loss carryforwards when they reverse in future periods, both of which resulted from the enactment of the Tax Act.

During the year ended December 31, 2017, in its assessment of the realizability of deferred tax assets, the Company concluded that $2.4 million of the $8.4 million of deferred tax liabilities recorded for indefinite-lived IPR&D as of December 31, 2017 could be considered a source of future taxable income for the realization of deferred tax assets. As a result, the Company did not use $6.0 million of the established deferred tax liabilities to reduce the valuation allowance recorded as of December 31, 2017 because the reversal of that portion of the deferred tax liabilities could not be assumed to occur.

The Company had not recorded any amounts for unrecognized tax benefits as of December 31, 2018 and 2017. The Company files income tax returns in the U.S. and Massachusetts. The federal and state returns are generally subject to tax examinations for the tax years ended December 31, 2013 to the present. There are currently no pending tax examinations. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service and state tax authorities to the extent utilized in a future or prior period. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

13. Net Loss per Share

Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2018	2017
Numerator:		
Net loss	$ (97,395)	$ (66,443)
Accretion of redeemable convertible preferred stock to redemption value	(644)	(719)
Net loss attributable to common stockholders	$ (98,039)	$ (67,162)
Denominator:		
Weighted average common shares outstanding—basic and diluted	26,945,508	7,756,180
Net loss per share attributable to common stockholders—basic and diluted	$ (3.64)	$ (8.66)

The Company excluded 372,301 shares and 733,134 shares of restricted common stock, presented on a weighted average basis, from the calculations of basic net loss per share attributable to common stockholders for the years ended December 31, 2018 and 2017, respectively, because those shares had not vested.

The Company's potentially dilutive securities, which include stock options, unvested restricted common stock and redeemable convertible preferred stock, have been excluded from the computation of diluted net loss per share attributable to common stockholders as the effect would be to reduce the net loss per share. Therefore, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

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

	Year Ended December 31,	
	2018	2017
Options to purchase common stock	6,236,006	4,364,916
Unvested restricted common stock	219,148	526,478
Redeemable convertible preferred stock (as converted to common stock)	—	25,612,109
	6,455,154	30,503,503

In addition to the potentially dilutive securities noted above, as of December 31, 2017, the Company was obligated to issue common stock to Shire upon the occurrence of specified events (see Notes 4 and 5). Because the necessary conditions for issuance of the shares had not been met as of December 31, 2017, the Company excluded these shares from the table above and from the calculations of diluted net loss per share for the year ended December 31, 2017.

14. Commitments and Contingencies

Lease Commitments

The Company leases office and laboratory space under an operating lease that expires in April 2028. The Company recognizes rent expense on a straight-line basis over the respective lease period and has recorded deferred rent for rent expense incurred but not yet paid. The Company recorded rent expense of $3.0 million and $3.1 million during the years ended December 31, 2018 and 2017, respectively.

In May 2015, the Company entered into an operating lease for office and laboratory space in Cambridge, Massachusetts, which was due to expire in May 2022. In connection with entering into this lease agreement, the Company issued a letter of credit collateralized by cash deposits totaling $1.0 million, which was reduced to $0.7 million in December 2017. These cash deposits are classified as restricted cash on the consolidated balance sheets. In September 2017, the Company and the lessor agreed to early terminate the lease as of April 2018 and the Company was relieved of its obligation to pay the remaining lease payments through the expiration date of the original lease. The Company vacated the leased space in April 2018 and the letter of credit was released during the third quarter of 2018.

Pursuant to the Shire Agreement (see Note 4), in December 2016, the Company assumed an operating lease, due to expire in May 2018, for office and laboratory space in Lexington, Massachusetts. In January 2017, in connection with this lease agreement, the Company issued two letters of credit collateralized by cash deposits totaling $0.3 million, which were classified as restricted cash on the consolidated balance sheets. In November 2017, the lease was amended pursuant to which (i) the lease was extended by 12 months, commencing in June 2018 and expiring in May 2019, and (ii) the landlord was granted the option, at its sole discretion, to terminate the lease upon 90 days' notice, provided that the expiration date will be no earlier than November 30, 2018. On June 22, 2018 the Company entered into a Termination and Surrender Agreement with the landlord relating to this lease subject to certain conditions. In July 2018, following receipt of a $0.3 million termination payment, the landlord released the Company from any further obligations under the lease. The Company vacated the leased space in June 2018 and the letters of credit were released during the third quarter of 2018.

In June 2017, the Company entered into an operating lease for office and laboratory space at its new headquarters in Lexington, Massachusetts. Monthly lease payments include base rent charges of $0.2 million, which are subject to a 3% annual increase each year. The lease expires in April 2028. In June 2017, in connection with this lease agreement, the Company issued a letter of credit collateralized by cash deposits of $1.0 million, which are classified as restricted cash on the consolidated balance sheets as of December 31, 2018 and 2017.

The following table summarizes the future minimum lease payments due under the Company's operating leases as of December 31, 2018 (in thousands):

Year Ending December 31,		
2019	$	2,534
2020		2,610
2021		2,688
2022		2,769
2023		2,852
2024 and thereafter		13,096
	$	26,549

Research, Supply and License Agreements

Pursuant to the Shire Agreement (see Note 4), in December 2016, the Company was assigned and assumed several contracts related to the MRT Program. The material agreements that were assigned to and assumed by the Company in connection with the acquisition are described below.

Roche Master Supply Agreement

The Company is a party to a master supply agreement with Roche Diagnostics Corporation ("Roche") pursuant to which Roche will custom manufacture certain products for the Company. The agreement requires the Company to purchase from Roche specified manufactured products and the related raw materials in an amount equal to the greater of (i) quantities of raw materials in the Company's annual forecast to be purchased or (ii) 80% of the Company's demand for products as the same or similar type (the "Purchase Commitment"). In June 2017, the Company exercised its option under the agreement to extend the agreement through December 31, 2024. On September 28, 2018, the Company and Roche amended the agreement to remove and replace the Purchase Commitment for certain manufactured products and related raw materials supplied by Roche. The agreement, as amended, specifies a minimum purchase requirement for certain custom manufactured products. As of December 31, 2018, the Company's purchase commitments under the agreement totaled $24.0 million, with $9.6 million committed as payments in 2019, $0.5 million committed as payments in 2020 and $3.5 million committed as payments each year from 2021 to 2024. Research and development expenses related to this agreement totaled $5.0 million and $1.8 million during the years ended December 31, 2018 and 2017, respectively.

MIT Research Agreement

The Company is a party to a research agreement with the Massachusetts Institute of Technology ("MIT") pursuant to which the Company is obligated to reimburse MIT in an amount up to $3.1 million for specified direct and indirect costs incurred through October 2019 in specified research activities conducted for the Company. As of December 31, 2018 and 2017, the Company had paid MIT $2.5 million and $1.0 million, respectively, of the total committed amount. As of December 31, 2018, the Company's research commitments under the agreement totaled $0.7 million. Research and development expenses related to this agreement totaled $1.2 million during each of the years ended December 31, 2018 and 2017. As of December 31, 2018 and 2017, amounts payable by the Company under the agreement totaled $0 and $0.2 million, respectively.

As amended, the agreement expires in October 2019 and may be extended thereafter by mutual agreement of the parties.

MIT Exclusive Patent License Agreement

The Company is a party to an exclusive patent license agreement with MIT pursuant to which the Company received an exclusive license under the licensed patent rights to develop, manufacture and commercialize any product containing both (i) any RNA sequences, including mRNA, that encode a protein or peptide suitable for human therapeutic use which may include operably linked non-coding sequences that facilitate translation of the coding portion of such RNA sequence, but such non-coding sequences do not include nucleic acids that function through an RNA interface mechanism or transcriptional activation mechanism (the "coding RNA component"), and (ii) products covered by the licensed patent rights (the "lipid products"). A product containing both a coding RNA component and a lipid product is referred to as a "licensed product." Under the licensed patent rights, the Company is permitted to develop, manufacture and commercialize the licensed products for the delivery of coding RNA components to treat disease in humans.

The Company has the right to grant sublicenses under this license. The patent rights licensed to the Company by MIT include claims that cover the Company's customized lipid-based nanoparticles used for delivery of coding RNA components in its MRT platform and MRT5201.

Under the license agreement, the Company is obligated to make annual license maintenance payments to MIT, payable on January 1 of each calendar year, of up to $0.2 million, which may be credited against royalties subsequently due on net sales of licensed products earned in the same calendar year. During each of the years ended December 31, 2018 and 2017, the Company paid annual license maintenance fees of $0.1 million to MIT.

The Company is also obligated to make milestone payments to MIT aggregating up to $1.375 million upon the achievement of specified clinical and regulatory milestones with respect to each licensed product and $1.250 million upon the Company's first commercial sale of each licensed product, and to pay royalties of a low-single-digit percentage to MIT based on the Company's, and any of its affiliates' and sublicensees', net sales of licensed products. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances. The Company's obligation to make royalty payments extends with respect to a licensed product in a country until the expiration of the last-to-expire patent or patent application licensed from MIT covering the licensed product in the country. In addition, the Company is obligated to pay MIT a low-double-digit percentage of the portion of income from sublicenses that the Company ascribes to the MIT-licensed patents, excluding royalties on net sales and research support payments. In 2019, pursuant to such provision, the Company has agreed to pay $0.7 million to MIT as its share of sublicense income with respect to the upfront payment received under the Sanofi Agreement, which is recorded in accrued expenses on the Company's consolidated balance sheet as of December 31, 2018. The amounts that the Company may owe to MIT will depend upon the relative value of the patents the Company licensed from MIT and sublicensed to Sanofi as compared to the other rights that the Company licensed to Sanofi. The determination of the relative value of such rights is subject to a process described in the Company's license agreement with MIT (see Note 3).

The agreement obligates the Company to use commercially reasonable efforts and expend a minimum amount of resources each year to develop licensed products in accordance with a development plan, and a development milestone timetable specified in the agreement; to use commercially reasonable efforts to commercialize licensed products; and upon commercialization, to make the licensed products reasonably available to the public.

MIT has the right to terminate the agreement if the Company fails to pay amounts when due or otherwise materially breaches the agreement and fails to cure such nonpayment or breach within specified cure periods or in the event the Company ceases to carry on its business related to the agreement. In the event of a termination due to the Company's breach caused by a due diligence failure of a licensed product, but where the Company has fulfilled its obligations with respect to a different licensed product, MIT may not terminate the agreement with respect to the different licensed product. MIT may immediately terminate the agreement if the Company or any of its affiliates brings specified patent challenges against MIT or assists others in bringing a patent challenge against MIT. The Company has the right to terminate the agreement for its convenience at any time on three months' prior written notice to MIT and payment of all amounts due to MIT through the date of termination.

The Company's patent rights, and the rights of its affiliates and sublicensees, in specified licensed products may also terminate, if, after November 1, 2018, the Company, its affiliates or MIT receives a request from a third party to develop such licensed product for which the Company is unable to, within nine months of receiving notice of any such request, either demonstrate that the Company has initiated a fully funded project for the commercial development of such licensed product, and provide a business plan with acceptable milestones; demonstrate that the licensed product proposed by such third party would be competitive with a licensed product for which the Company has initiated a fully funded project; or enter into a sublicense agreement with such third party on commercially reasonable terms, and, in each case, MIT, in its sole discretion, grants a license to such third party for the specified patent rights.

Research and development expenses related to this agreement totaled $0.1 million during each of the years ended December 31, 2018 and 2017. As of December 31, 2018 and 2017, amounts payable by the Company related to this agreement totaled $0.7 million and $0, respectively.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases,

unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2018 and 2017.

Legal Proceedings

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities.

15. Related Party Transactions

Consulting Agreement with Daniel S. Lynch

In 2012, the Company entered into a consulting agreement with Daniel S. Lynch, the chairman of the Company's board of directors, for the provision of consulting, advisory and related services. Pursuant to the consulting agreement, as amended through March 2015, Mr. Lynch was entitled to base compensation of $100,000 per year and was eligible to receive an annual performance bonus of up to 25% of his base compensation. In June 2018, the Company's board of directors approved a director compensation program that became effective on the effective date of the registration statement related to the Company's IPO. The Company has not made any payments to Mr. Lynch under the consulting agreement since the approval of the director compensation program. During each of the years ended December 31, 2018 and 2017, the Company recorded general and administrative expenses of $0.1 million related to this agreement. During each of the years ended December 31, 2018 and 2017, the Company paid Mr. Lynch $0.1 million in connection with his services provided under the agreement. As of December 31, 2018 and 2017, amounts due under this agreement totaled $11,250 and $20,000, respectively, which were included in accrued expenses on the consolidated balance sheets.

During the year ended December 31, 2017, the Company granted to Mr. Lynch stock options to purchase 85,170 shares of common stock, at an exercise price of $7.39 per share, which vest monthly over a four-year period. The stock options had a grant-date fair value of $4.06 per share and an aggregate fair value of $0.3 million.

16. Costs Associated with Restructuring

In June 2017, the Company implemented a reorganization of its operations, which reduced its workforce by 17 positions in connection with a strategic realignment of resources aimed at better supporting the advancement of its MRT platform. The benefits provided to the employees as part of this reorganization were determined to be involuntary termination benefits provided under the terms of a one-time benefit arrangement pursuant to which employees were not required to provide future services to the Company. During the year ended December 31, 2017, the Company recorded employee severance charges of $0.5 million related to this restructuring, which were included in research and development expenses in the consolidated statements of operations.

Changes in accrued restructuring costs were as follows (in thousands):

Balance at December 31, 2016	$ —
Charges	473
Payments	(473)
Balance at December 31, 2017	$ —

17. Benefit Plans

The Company has established a defined-contribution retirement plan under Section 401(k) of the Code. This plan covers all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the plan may be made at the discretion of the Company's board of directors. During the years ended December 31, 2018 and 2017, the Company contributed $0.3 million and $0.2 million, respectively, to the plan.

18. Selected Quarterly Financial Information (Unaudited)

The following table contains quarterly financial information for 2018 and 2017 (in thousands, except per share amounts). The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2018				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue	$ —	$ —	$ 238	$ 1,182	$ 1,420
Total operating expenses	22,389	29,062	45,719	8,480	105,650
Loss from operations	(22,389)	(29,062)	(45,481)	(7,298)	(104,230)
Net loss	(21,209)	(27,503)	(42,646)	(6,037)	(97,395)
Net loss per share applicable to common stockholders—basic and diluted	$ (2.35)	$ (3.04)	$ (0.97)	$ (0.13)	$ (3.64)

	2017				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue	$ —	$ —	$ —	$ —	$ —
Total operating expenses	14,869	18,955	20,836	24,588	79,248
Loss from operations	(14,869)	(18,955)	(20,836)	(24,588)	(79,248)
Net loss	(13,954)	(17,933)	(18,465)	(16,091)	(66,443)
Net loss per share applicable to common stockholders—basic and diluted	$ (1.86)	$ (2.36)	$ (2.40)	$ (2.04)	$ (8.66)

Due to a clerical error in the computation of the net loss attributable to common stockholders, the Company reported the net loss per share applicable to common stockholders—basic and diluted for the three months ended June 30, 2018 and 2017 as $2.94 and $2.31, respectively, in the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2018. The net loss per share applicable to common stockholders—basic and diluted for the second quarters ended June 30, 2018 and 2017 is $3.04 and $2.36, respectively, as shown in the chart above. The Company concluded that this error was not material to the periods impacted.

During the three months ended December 31, 2018, the fair value of contingent consideration decreased by $14.6 million as a result of an increase in the discount rate (see Note 5).

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-226047) of Translate Bio, Inc. of our report dated March 21, 2019 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 21, 2019

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ronald C. Renaud, Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K of Translate Bio, Inc.;

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

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

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

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

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

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

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

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

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

Date: March 21, 2019

By: /s/ Ronald C. Renaud, Jr.
Ronald C. Renaud, Jr.
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John R. Schroer, certify that:

1. I have reviewed this Annual Report on Form 10-K of Translate Bio, Inc.;

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

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

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

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

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

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

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

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

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

Date: March 21, 2019

By: /s/ John R. Schroer
John R. Schroer
Treasurer and Chief Financial Officer

Exhibit 32.1

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

In connection with this Annual Report on Form 10-K of Translate Bio, Inc. (the "Company") for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Annual Report"), the undersigned, Ronald C. Renaud, President and Chief Executive Officer, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

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

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

Date: March 21, 2019

By: /s/ Ronald C. Renaud, Jr.
Ronald C. Renaud, Jr.
President and Chief Executive Officer

Exhibit 32.2

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

In connection with this Annual Report on Form 10-K of Translate Bio, Inc. (the "Company") for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Annual Report"), the undersigned, John R. Schroer, Treasurer and Chief Financial Officer, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

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

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

Date: March 21, 2019

By: /s/ John R. Schroer
John R. Schroer
Treasurer and Chief Financial Officer