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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: 001-38670

LogicBio Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**47-1514975**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification Number)**

99 Erie St.
Cambridge, MA 02139
(617) 245-0399
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	**Nasdaq Global Market**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities 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 the 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 the 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, a 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. (Check one):

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 ☒

There was no aggregate market value of shares of common stock held by non-affiliates of the registrant as of June 30, 2018, the last business day of the registrant's most recently completed second fiscal quarter, because the registrant's common stock was not trading on any exchange on that date.

As of March 31, 2019, there were 22,348,728 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2019 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect," or similar expressions, or the negative or plural of these words or expressions. These forward-looking statements include statements concerning the following:

- the initiation, cost, timing, progress and results of our current and future research and development activities and preclinical studies and potential future clinical trials;
- potential attributes and benefits of our GeneRide technology platform and our product candidates;
- our ability to take advantage of the modular nature of our GeneRide platform to simplify and accelerate development of new product candidates;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- the timing of, and our ability to obtain and maintain, regulatory approvals for our product candidates;
- our ability to quickly and efficiently identify and develop additional product candidates;
- our ability to advance any product candidate into and successfully complete clinical trials;
- our intellectual property position, including with respect to our trade secrets and the duration of our patent protection; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A, "Risk Factors," herein and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources and we have not independently verified the data from third party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors." These and other factors could cause our future performance to differ materially from our assumptions and estimates.

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to "LogicBio," "LogicBio Therapeutics Inc.," "the Company," "we," "us," "our" and similar references refer to LogicBio Therapeutics Inc. and its wholly owned subsidiaries. This Annual Report on Form 10-K also contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PART I

Item 1. Business.

Overview

We are a genome editing company focused on developing medicines to durably treat rare diseases in patients with significant unmet medical need using GeneRide, our proprietary technology platform. Our GeneRide technology is designed to precisely integrate corrective genes into a patient's genome to provide a stable therapeutic effect. Because GeneRide is designed to have this durable therapeutic effect, we are initially targeting rare liver disorders in pediatric patients where it is critical to provide treatment early in a patient's life before irreversible disease pathology can occur. We have demonstrated proof of concept of our therapeutic platform in animal models for a number of diseases and are focusing on our lead product candidate, LB-001, for the treatment of Methylmalonic Acidemia, or MMA, a life-threatening disease that presents at birth.

GeneRide is our genome editing technology that harnesses homologous recombination, or HR, a naturally occurring DNA repair process that maintains the fidelity of the genome. We believe that by using HR, GeneRide will allow us to insert therapeutic genes, known as transgenes, into specific targeted genomic locations without using exogenous nucleases, which are enzymes engineered to cut DNA. GeneRide-directed transgene integration is designed to leverage endogenous promoters at these targeted locations to drive high levels of tissue-specific gene expression, without the detrimental issues that have been associated with the use of exogenous promoters.

We believe that GeneRide offers several key potential advantages over gene therapy and gene editing technologies that rely on exogenous promoters and nucleases. By harnessing the naturally occurring process of HR, GeneRide does not face the same challenges associated with gene editing approaches that rely on engineered bacterial nuclease enzymes. The use of these enzymes has been associated with significantly increased risk of unwanted and potentially dangerous modifications in the host cell's DNA, which can lead to an increased risk of tumor formation. Furthermore, in contrast to conventional gene therapy, GeneRide is intended to provide precise, site-specific, stable and durable integration of a corrective gene into the chromosome of a host cell. In preclinical animal studies with GeneRide constructs, we have observed integration of the corrective gene in a specific location in the genome. This gives it the potential to provide a more durable approach than gene therapy technologies that do not integrate into the genome and lose their effect as cells divide. We believe these benefits make GeneRide well-positioned to treat genetic diseases, particularly in pediatric patients.

We believe our modular approach will allow GeneRide to deliver robust, tissue-specific gene expression that will be reproducible across different therapeutics delivered to the same tissue. By substituting a different transgene within the GeneRide construct, we believe we can deliver that transgene to address a new therapeutic indication while substantially maintaining all other components of the construct. We expect this approach will allow us to leverage common manufacturing processes and analytics across our future GeneRide product candidates and could potentially shorten the development process of future programs.

Beyond LB-001, we intend to develop additional product candidates for other indications based on ongoing research and development work we perform in our own laboratories, as well as the work of our academic partners. The criteria for selecting these proposed product candidates are initially:

- **Genetically defined disease.** As with LB-001, we expect our future product candidates to target disorders associated with genetically defined mechanisms.
- **High unmet need in pediatric patients.** Because GeneRide is designed to deliver therapeutic durability, we intend to provide lifelong benefit to patients by intervening early in their lives with a treatment that restores the function of aberrant genes before irreversible declines in function can occur.
- **Liver expression.** Because of the modularity of our platform in creating new product candidates in the same tissue, we will initially focus on developing therapies for indications that can be addressed by

targeting the liver. We intend to evaluate the tolerability, effective targeting and expression of our therapy in our lead program in MMA, as well as our next few product candidates, before deploying additional potential therapies based on GeneRide in other tissues.

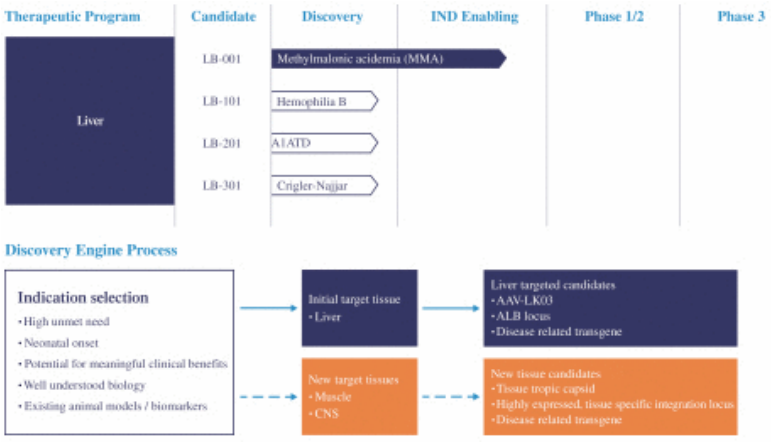
We expect that the initial product candidates we develop, including LB-001, will address diseases by targeting the liver, including a category of diseases known as inborn errors of metabolism, a group of genetic disorders that disrupt normal metabolic processes. Our intent is to deliver transgenes for these disorders using a GeneRide construct designed to integrate immediately behind the gene coding for albumin, the most highly expressed gene in the liver. Expression of the transgenes "piggybacks" on the expression of albumin, which we believe will provide sufficient therapeutic levels of desirable proteins given the high level of albumin expression in the liver. We have developed GeneRide utilizing certain core technology licensed from Stanford University and the University of Texas.

Based on our GeneRide technology, we are developing our lead product candidate, LB-001, to treat MMA. We plan to advance LB-001 to an IND filing by the end of 2019 and into a Phase 1/2 clinical trial in pediatric MMA patients in 2020. We believe that achieving clinical proof of concept in an inherited liver disease such as MMA will validate our platform technology, including its potential application to other organs and diseases. In addition to MMA, we have demonstrated proof of concept of our platform in hemophilia B, alpha-1-antitrypsin deficiency, or A1ATD, and Crigler-Najjar syndrome animal disease models. We expect to select future product candidates from these genetic diseases or others addressed by targeting the liver initially, and later by targeting the central nervous system, or CNS, and muscle.

Our proprietary GeneRide technology platform is based on research conducted by leading gene therapy scientists at the Kay Lab at Stanford University, and we have assembled a world-class team of executives, founders and advisors with years of highly relevant experience to enable the development of our genome editing platform and the advancement of our product candidates for patients with significant unmet medical needs. Led by Frederic (Fred) Chereau, our Chief Executive Officer, our team's expertise spans gene therapy, HR, rare disease drug discovery and development, technical development, clinical and regulatory strategy, manufacturing strategy and operations, as well as business strategy, intellectual property and finance. Members of this team have been involved in developing therapies for rare diseases in both large and small biotechnology companies including Genzyme, Shire, Novartis, aTyr Pharma, Synlogic and Millennium Pharmaceuticals. Collectively, members of the team have contributed to the development of an array of approved drugs, most of which are treatments for rare diseases.

We have also established an extensive network of advisors and consultants with expertise across many critical areas of our business, from drug design, manufacturing and clinical development to regulatory approval. Our consultants and advisors possess deep experience in adeno-associated virus, or AAV, capsid development, mechanisms of DNA repair and delivery technologies, which complements our internal capabilities and supports our efforts in the development of our GeneRide-based product candidates. Additionally, our management team is actively supported by a scientific advisory board, or SAB, which includes our co-founders, Drs. Mark Kay, Adi Barzel and Leszek Lisowski, and experts such as Drs. Markus Grompe and Fraser Wright. We believe that our SAB's expertise, combined with our network of consultants and advisors, is a pivotal asset for our product development efforts. We are also supported by leading life sciences investors, including OrbiMed, Arix Bioscience, Andera Partners (formerly, Edmond de Rothschild Investment Partners), Pontifax and SBI Holdings. We are committed to bringing much-needed therapies to children with serious genetic deficiencies and we work closely with patient foundations, such as the Organic Acidemia Association.

Below is a summary of our ongoing discovery, research and development programs, as well as our discovery process using GeneRide:



Strategy

Our mission is to transform the lives of patients living with devastating genetic diseases by building the leading integrated genetic medicine company focused on developing and commercializing potentially curative therapeutics based on our GeneRide platform. Key elements of our strategy are to:

- **Advance LB-001 through successful clinical trials and ultimately into commercialization.** We chose a specific organic acidemia, MMA, as our initial indication to enter proof-of-concept trials in humans due to the high unmet medical need and the absence of therapeutic treatments for this disease. We plan to advance our lead product candidate, LB-001 to an IND filing by the end of 2019 and into a Phase 1/2 clinical trial in pediatric MMA patients in 2020. Our goal is to develop LB-001 ourselves and, if approved, to retain global commercialization rights and commercialize through a small, targeted sales organization.
- **Aggressively pursue additional indications addressed by targeting the liver.** For our initial animal proof-of-concept studies, we selected liver diseases with significant unmet medical need and well-validated targets with accepted disease-correlated biomarkers, and where we believe the GeneRide platform can provide unique benefits by addressing the root cause of the disease. We plan to select at least one new indication from our preclinical portfolio by the end of 2019 and move diligently into IND-enabling studies utilizing our modular approach and leveraging learnings from our lead program.
- **Collaborate to realize the full potential of GeneRide.** We plan to leverage strategic partnerships to accelerate advancement of our programs by accessing non-dilutive capital and disease-specific expertise in indications outside of our initial core focus. These indications could include other diseases addressable by targeting the liver, such as blood clotting disorders and lysosomal storage diseases. We also intend to seek collaborations to accelerate the development of the GeneRide platform in new tissues, such as the CNS and muscle.
- **Build an exceptional team and organization.** Delivering on the promise of a potential breakthrough technology like GeneRide requires an exceptional organization. We have assembled a group of leaders and scientific talent in the fields of rare diseases, genome editing and gene therapy with notable additions over the past quarter, and expect to continue building and expanding our team, as required, to execute on our plans to develop and commercialize genetic medicines.

- **Maintain our scientific leadership in the field of genome editing.** We will strive to continue optimizing all aspects of our GeneRide technology through a combination of in-house research and work by our network of academic collaborators. Additionally, we expect to invest in the development of next-generation AAV vectors that we hope will continue to enhance the utility of our GeneRide platform, and provide us with AAV assets for potential out-licensing opportunities to companies developing conventional gene therapy products. The collaboration with the Children's Medical Research Institute, or CMRI, announced in November 2018, is a prime example of our efforts. We believe that our scientific leadership will provide us opportunities to expand our intellectual property portfolio.

Genetic Diseases and Their Treatment

There is a subset of human diseases that can be traced to changes in the DNA that are either inherited or acquired early in embryonic development. Of particular interest for developers of genetic therapies are diseases caused by a mutation in a single gene, known as monogenic diseases. There are believed to be over 6,000 monogenic diseases. Typically, any particular genetic disease caused by inherited mutations is relatively rare, but taken together, the toll of genetic-related disease is high. Well-known genetic diseases include cystic fibrosis, Duchenne muscular dystrophy, Huntington's disease and sickle cell disease. Other classes of genetic diseases include metabolic disorders, such as organic acidemias, and lysosomal storage diseases where dysfunctional genes result in defects in metabolic processes and the accumulation of toxic byproducts that can lead to serious morbidity and mortality both in the short-term and long-term.

Monogenic diseases have been of particular interest for biomedical innovators due to the perceived simplicity of their disease pathology. However, the vast majority of these diseases and disorders remain unaddressed, though this is beginning to change, largely due to innovation in two fields: gene therapy and gene editing.

Gene Therapy

Gene therapies alter the gene expression profile of a patient's cells by gene transfer, a process of delivering a therapeutic gene, called a transgene. Drug developers use modified viruses as vectors to transport transgenes into the nucleus of a cell to alter or augment the cell's capabilities. Developers have made great strides in introducing genes into cells in tissues such as the liver, the retina of the eye and the blood-forming cells of the bone marrow using a variety of vectors. These approaches have in some cases led to approved therapies and, in other cases, have shown very promising results in clinical trials.

There are multiple gene therapy approaches currently being used to treat patients. In conventional AAV gene therapy, the transgene is introduced into the nucleus of the host cell, but is not intended to integrate in chromosomal DNA. The transgene is expressed from a non-integrated genetic element called an episome that exists inside the nucleus. A second type of gene therapy employs the use of a different type of virus, such as lentivirus, that inserts itself, along with the transgene, into the chromosomal DNA but at arbitrary sites.

Episomal expression of a gene must be driven by an exogenous promoter, leading to production of a protein that corrects or ameliorates the disease condition. We believe that this type of gene therapy will be most successful when genes are delivered into tissues that consist of stable, rather than rapidly dividing, cells.

Limitations of Gene Therapy

- **Dilution effects as cells divide and tissues grow.** In the case of gene therapy based on episomal expression, when cells divide during the process of growth or tissue regeneration, the benefits of the therapy typically decline because the transgenes were not intended to integrate into the host chromosome, thus not replicated during cell division. Each new generation of cells thus further reduces the proportion of cells expressing the transgene in the target tissue, leading to the reduction or elimination of the therapeutic benefit over time.

- **Inability to control site of insertion.** While the use of some gene therapy using viral mediated insertion has the potential to provide long-term benefit because the gene is inserted into the host chromosome, there is no ability to control where the gene is inserted, which presents a risk of disrupting an essential gene or inserting into a location that can promote undesired effects such as tumor formation. For this reason, these integrating gene therapy approaches are primarily limited to *ex vivo* approaches, where the cells are treated outside the body and then re-inserted.
- **Use of exogenous promoters increases the risk of tumor formation.** A common feature of both gene therapy approaches is that the transgene is introduced into cells together with an exogenous promoter. Promoters are required to initiate the transcription and amplification of DNA to messenger RNA, or mRNA, which will ultimately be translated into protein. Expression of high levels of therapeutic proteins from a gene therapy transgene requires strong, engineered promoters. While these promoters are essential for protein expression, previous studies conducted by others in animal models have shown that non-specific integration of gene therapy vectors can result in significant increases in the development of tumors. The strength of the promoters plays a crucial role in the increase of the development of these tumors. Thus, attempts to drive high levels of expression with strong promoters may have long-term deleterious consequences.

Gene Editing

Gene editing is the deletion, alteration or augmentation of aberrant genes by introducing breaks in the DNA of cells using exogenously delivered gene editing mechanisms. Most current gene editing approaches have been limited in their efficacy due to high rates of unwanted on- and off-target modifications and low efficiency of gene correction, resulting in part from the cell trying to rapidly repair the introduced DNA break. The current focus of gene editing is on disabling a dysfunctional gene or correcting or skipping an individual deleterious mutation within a gene. Due to the number of possible mutations, neither of these approaches can address the entire population of mutations within a particular genetic disease, as would be addressed by the insertion of a full corrective gene.

Unlike the gene therapy approach, gene editing allows for the repaired genetic region to propagate to new generations of cells through normal cell division. Furthermore, the desired protein can be expressed using the cell's own regulatory machinery. The traditional approach to gene editing is nuclease-based, and it uses nuclease enzymes derived from bacteria to cut the DNA at a specific place in order to cause a deletion, make an alteration or apply a corrective sequence to the body's DNA.

Once nucleases have cut the DNA, traditional gene editing techniques modify DNA using two routes: homology-directed repair, or HDR, and non-homologous end joining, or NHEJ. HDR involves highly precise incorporation of correct DNA sequences complementary to a site of DNA damage. HDR has key advantages in that it can repair DNA with high fidelity and it avoids the introduction of unwanted mutations at the site of correction. NHEJ is a less selective, more error-prone process that rapidly joins the ends of broken DNA, resulting in a high frequency of insertions or deletions at the break site.

Nuclease-Based Gene Editing

Nuclease-based gene editing uses nucleases, enzymes that were engineered or initially identified in bacteria that cut DNA. Nuclease-based gene editing is a two-step process. First, an exogenous nuclease, which is capable of cutting one or both strands in the double-stranded DNA, is directed to the desired site by a synthetic guide RNA and makes a specific cut. After the nuclease makes the desired cut or cuts, the cell's DNA repair machinery is activated and completes the editing process through either NHEJ or, less commonly, HDR.

NHEJ can occur in the absence of a DNA template for the cell to copy as it repairs a DNA cut. This is the primary or default pathway that the cell uses to repair double-stranded breaks. The NHEJ mechanism can be used

to introduce small insertions or deletions, known as indels, resulting in the knocking out of the function of the gene. NHEJ creates insertions and deletions in the DNA due to its mode of repair and can also result in the introduction of off-target, unwanted mutations including chromosomal aberrations.

Nuclease-mediated HDR occurs with the co-delivery of the nuclease, a guide RNA and a DNA template that is similar to the DNA that has been cut. Consequently, the cell can use this template to construct reparative DNA, resulting in the replacement of defective genetic sequences with correct ones. We believe the HDR mechanism is the preferred repair pathway when using a nuclease-based approach to insert a corrective sequence due to its high fidelity. However, a majority of the repair to the genome after being cut with a nuclease continues to use the NHEJ mechanism. The more frequent NHEJ repair pathway has the potential to cause unwanted mutations at the cut site, thus limiting the range of diseases that any nuclease-based gene editing approaches can target at this time.

The homology-directed and non-homologous end-joining DNA repair pathways used for genome editing are illustrated in the diagram below:

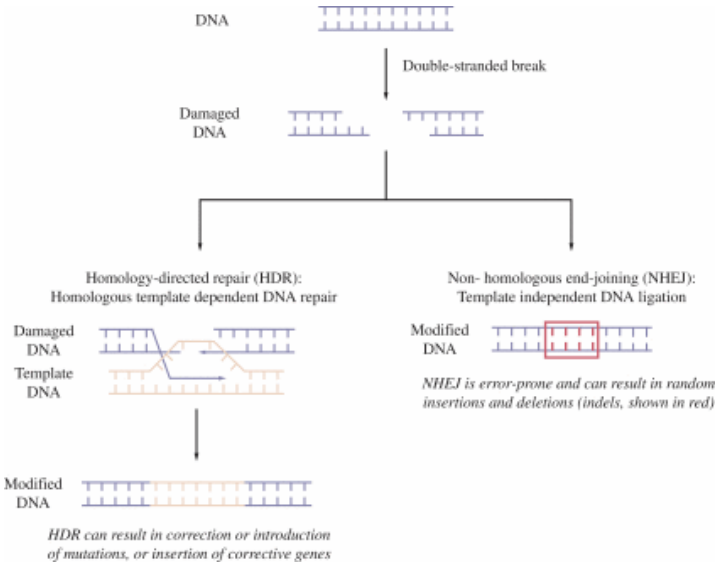


Figure 1. HDR and NHEJ DNA repair pathways.

Traditional gene editing has used one of three nuclease-based approaches: Transcription activator-like effector nucleases, or TALENs; Clustered, Regularly Interspaced Short Palindromic Repeats Associated protein-9, or CRISPR/Cas9; and Zinc Finger Nucleases, or ZFN. While these approaches have already contributed to significant advances in research and product development, we believe they have inherent limitations.

Limitations of Nuclease-Based Gene Editing

Nuclease-based gene editing approaches are limited by their use of bacterial nuclease enzymes to cut DNA and by their reliance on exogenous promoters for transgene expression. These limitations include:

- **Nucleases cause on- and off-target mutations.** Conventional gene editing technologies can result in genotoxicity, including chromosomal alterations, based on the error-prone NHEJ process and potential off-target nuclease activity.

- **Delivery of gene editing components to cells is complex.** Gene editing requires multiple components to be delivered into the same cell at the same time. This is technically challenging and currently requires the use of multiple vectors.
- **Bacterially derived nucleases are immunogenic.** Because the nucleases used in conventional gene editing approaches are mostly bacterially derived, they have a higher potential for immunogenicity, which in turn limits their utility.

Because of these limitations, gene editing has been primarily restricted to *ex vivo* applications in cells, such as hematopoietic cells.

Our GeneRide Technology Platform

Our proprietary GeneRide platform technology has the potential to overcome some of the key limitations of both traditional gene therapy and conventional gene editing approaches in a way that we believe is well-positioned to treat genetic diseases, particularly in pediatric patients. GeneRide uses an AAV vector to deliver a gene into the nucleus of the cell. It then uses HR to stably integrate the corrective gene into the genome of the recipient at a location where it is regulated by an endogenous promoter, leading to what we believe will be lifelong protein production, even as the body grows and changes over time, which is not feasible with conventional AAV gene therapy.

Genome Editing Using GeneRide: Mechanism and Attributes

We describe our approach as genome editing rather than gene editing because it uses HR to deliver the corrective gene to one specific location in the genome. GeneRide inserts the corrective gene in a precise manner, leading to site-specific integration in the genome. Our genome editing approach does not require the use of exogenous nucleases or promoters; instead, we leverage the cell's existing machinery to integrate and initiate transcription of therapeutic transgenes.

The illustration below shows how a GeneRide construct inserts a transgene at a specific point next to the albumin gene using HR:

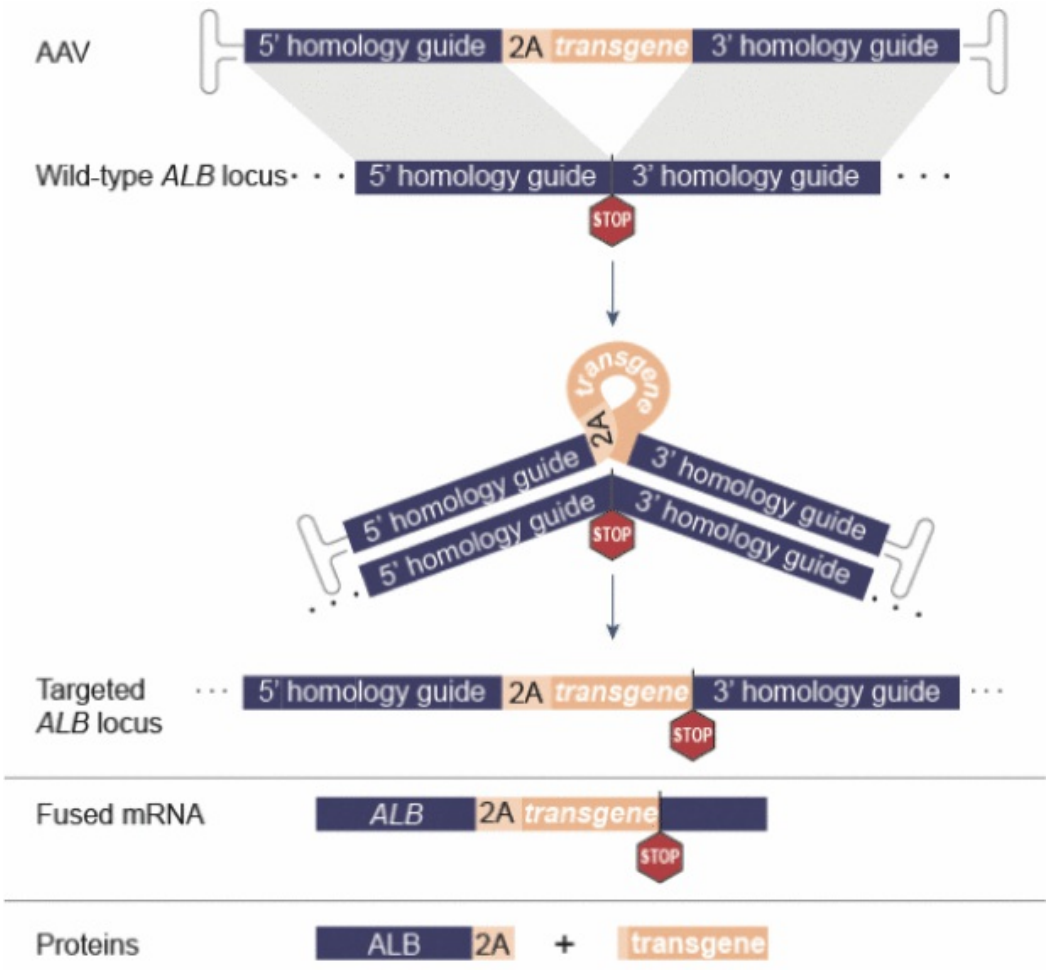


Figure 2. Schematic of the GeneRide construct before integration (AAV) and following HR-mediated integration into the genome at the targeted Albumin, or *ALB*, locus. Expression from the targeted locus results in the production of albumin and transgene, as separate proteins, at equivalent levels, which is coded for by the *ALB* gene.

The GeneRide technology consists of three fundamental components, each of which contributes to the potential benefits of the GeneRide approach:

- **Homology guides comprised of hundreds of nucleotides.** Our flanking sequences, known as homology guides, direct site-specific integration and limit off-target insertion of our construct. Each arm is hundreds of nucleotides long, in contrast to guide sequences used in CRISPR/Cas9, which are

only dozens of base pairs long, and we believe this increased length promotes improved precision and site-specific integration. GeneRide's homology guides direct the integration of the transgene immediately behind a highly expressed gene, which we have observed in animal models to result in high levels of expression without the need to introduce an exogenous promoter.

- **Transgene.** We choose corrective genes, known as transgenes, to integrate into the host cell's genome. These transgenes are the functional versions of the disease associated genes found in a patient's cells. We optimize the combined size of the transgenes and the homology guides to increase the likelihood that these transgenes are of a suitable sequence length to be efficiently packaged in the capsid, which we believe increases the likelihood that the transgenes will ultimately be delivered appropriately in the patient.
- **2A peptide for polycistronic expression.** We include a short sequence coding for a 2A peptide, which plays a number of important roles. First, the 2A peptide facilitates polycistronic expression, which is the production of two distinct proteins from the same mRNA. This, in turn, allows us to integrate our transgene in a non-disruptive way by coupling transcription of our transgene to a highly expressed target gene in the tissue of interest, driven by a strong endogenous promoter. For our liver-directed programs, including LB-001, we have chosen the albumin locus as the site of integration. Through a process known as ribosomal skipping, the 2A peptide facilitates production of the therapeutic protein at the same level as albumin in each modified cell. Second, the patient's albumin is produced normally, except for the addition of a C-terminal tag that serves as a circulating biomarker to indicate successful integration and expression of the transgene. We believe that this modification to albumin will have minimal effect on its function, based on the results of clinical trials of other albumin protein fusions that have been conducted by others. The 2A peptide has been incorporated into other potential therapeutics such as T cell receptor chimeric antigen receptors, or CAR-Ts.

A key step in applying the GeneRide platform is to identify the target genetic locus for integration. This is important because the location will dictate regulation of transgene expression, specifically the levels and tissues where the protein will be produced. For our liver-directed programs, including LB-001, we have selected the albumin locus as the site of integration.

Albumin is only produced at meaningful levels in the liver, where it is the most highly expressed gene. Integration of the transgene downstream of a highly expressed tissue-specific gene, like albumin, is an important feature of GeneRide. The following graphs show the expression of albumin relative to other genes in the liver and the expression of albumin in the liver compared to other tissues with the highest expression of albumin.

Top 2,000 liver expressed genes

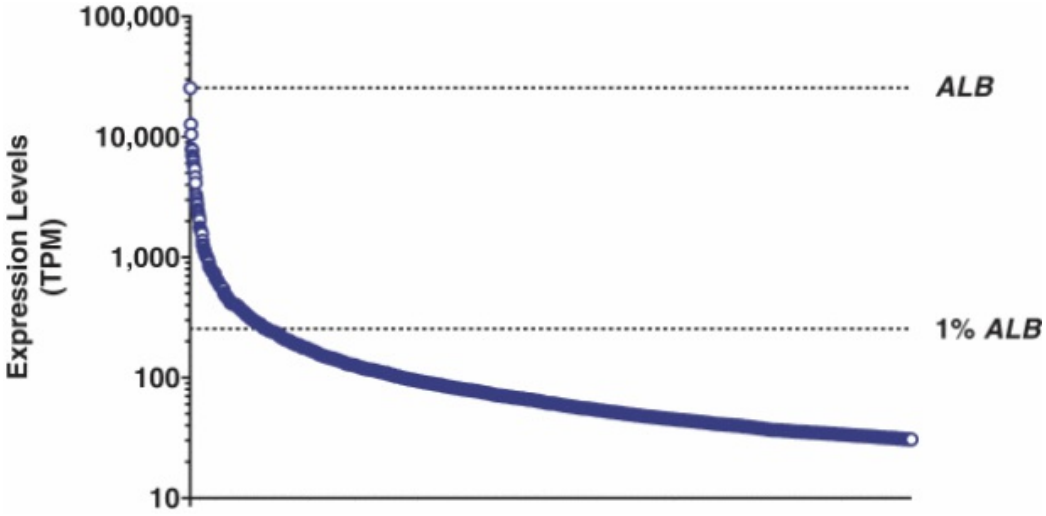


Figure 3. The most abundant genes expressed in the liver, ranked from highest (*ALB*) to number 2,000. Each circle represents an individual gene. Most genes in the liver are expressed at a small fraction of the levels of albumin. TPM=transcripts per million.

***ALB* gene expression across the 15 tissues with the highest *ALB* gene expression levels**

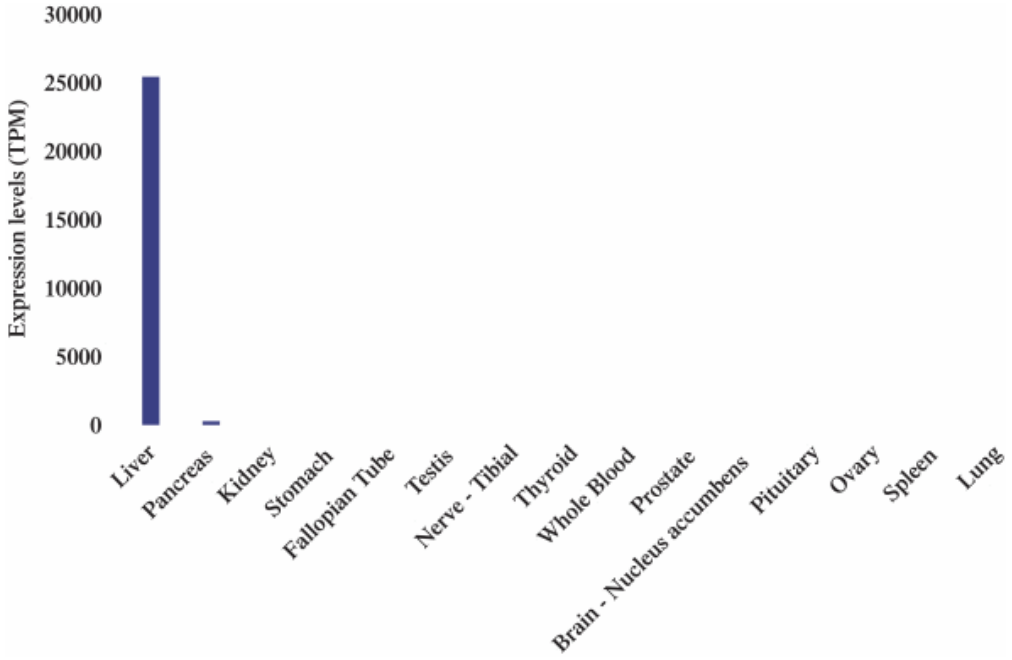


Figure 4. The liver is the organ where nearly all albumin is expressed in the body. Liver-specific GeneRide constructs targeting the *ALB* locus will predominantly be expressed in the liver.

Targeting the albumin locus allows us to leverage the strong endogenous promotor that drives the high level of albumin production to maximize the expression of our transgene. We believe that linking the expression of our transgene to albumin will allow the expression of our transgene at therapeutic levels without requiring the addition of exogenous promoters or the integration of our transgene in a majority of target cells.

This is supported by our data from animal models of MMA, hemophilia B and Crigler-Najjar syndrome. In these models, integration of the transgene into approximately 1% of cells resulted in therapeutic benefit. The strength of the albumin promoter overcomes the modest levels of integration to yield potentially therapeutic levels of transgene expression.

The following tables show the relative expression levels of albumin as compared to select disease-related genes in the liver, including methylmalonyl-CoA mutase, or *MUT*, the deficient gene in patients with MMA.

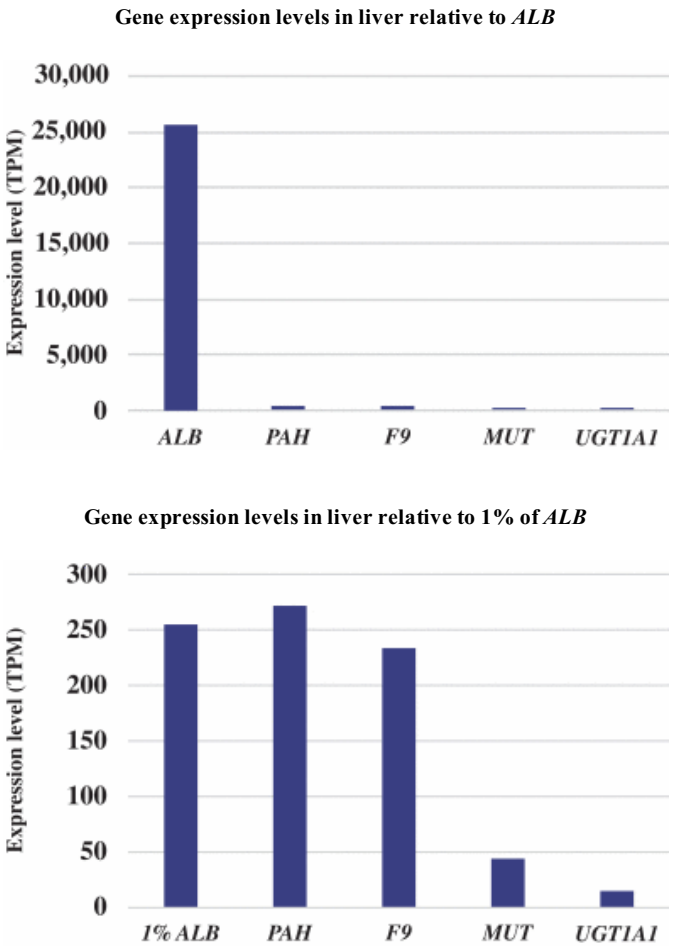
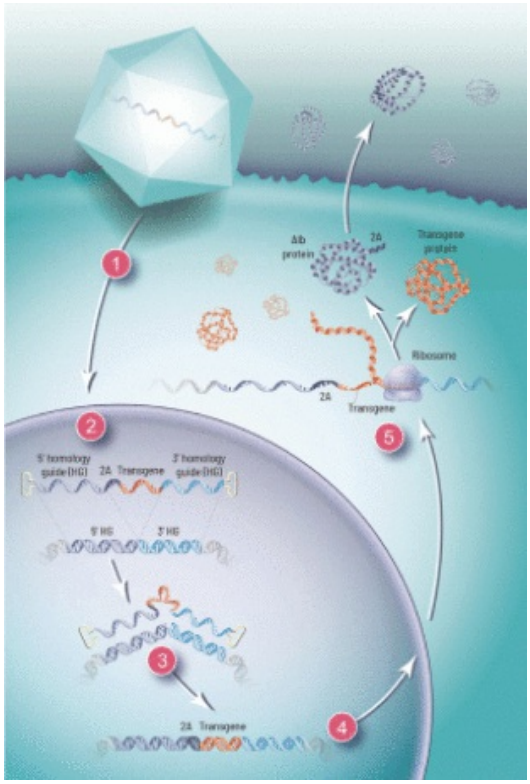


Figure 5. Albumin expression levels are 100x higher than other select liver genes associated with monogenic diseases. (*PAH*: phenylketonuria, *F9*: hemophilia B, *MUT*: MMA, *UGT1A1*: Crigler-Najjar syndrome).

We have observed that GeneRide leads to integration of the corrective gene at the albumin locus in preclinical mouse models of disease, non-human primates and human cells *(in vitro)*. In addition, the efficiency of HR that is required for transgene expression with GeneRide is enhanced at sites of active transcription and is likely to be low in tissue where albumin is not actively expressed. We expect that our future liver-directed product candidates will also target the albumin locus for integration. This feature should make both on-target and off-target integration a more predictable process across programs. In addition, because we are using HR, GeneRide product candidates do not contain any bacterial nucleases, addressing the risk of on-target or off-target integration into other sites that are associated with bacterial nucleases. We are exploring the possibility of

delivering our therapy to other tissues and target locations in the genome. In *in vitro* feasibility studies, GeneRide has been amenable to integration at other genomic positions, including rDNA, LAMA3 and COL7A1.

How GeneRide Works



First, we use a synthetic viral vector to deliver a transgene to the nuclei of the patient's cells via an infusion.

Two "homology guides," strands of DNA hundreds of nucleotides long that match a specific stretch of the patient's own genome, flank the transgene, as shown at (2) above.

Upon sensing the therapeutic DNA in the nucleus, the cell's natural DNA repair process is expected to activate and integrate the transgene at a specific site in the patient's genome, as shown at (3) above. GeneRide is designed to insert the transgene in a precise manner on the chromosome and at the gene that corresponds to the DNA sequence encoded in the homology guides. For our liver-targeted therapies, this specific location for integration is called the albumin locus.

When our therapeutic transgene is integrated at the albumin locus, it is designed to leverage the strength of this endogenous promoter to drive expression of the transgene, without disrupting albumin production, as shown at (4) above. By using an element called a 2A peptide, we believe we can efficiently produce albumin and the transgene as two separate proteins and further modify albumin in order to monitor GeneRide activity, as shown at (5) above.

Shortly after treatment, the modified cells can begin producing therapeutic levels of protein to combat the disease.

Potential advantages of our GeneRide approach include the following:

- **Targeted integration of transgene into the genome.** Conventional gene therapy approaches deliver therapeutic transgenes to target cells. A major shortcoming with most of these approaches is that once the genes are inside the cell, they do not integrate into the host cell's chromosomes and do not benefit from the natural processes that lead to replication and segregation of DNA during cell division. This is particularly problematic when conventional gene therapies are introduced early in the patient's life, because the rapid growth of tissues during the child's normal development will result in dilution and eventual loss of the therapeutic benefit associated with the transgene. Non-integrated genes expressed outside the genome on a separate strand of DNA are called episomes. This episomal expression can be effective in the initial cells that are transduced, some of which may last for a long time or for the life of a patient. However, episomal expression is typically transient in target tissues such as the liver, in which there is high turnover of cells and which tends to grow considerably in size during the course of a pediatric patient's life. With our GeneRide technology, the transgene is integrated into the genome, which has the potential to provide stable and durable transgene expression as the cells divide and the tissue of the patient grows, and may result in a durable therapeutic benefit.
- **Transgene expression without exogenous promoters.** With our GeneRide technology, the transgene is expressed at a location where it is regulated by a potent endogenous promoter. Specifically, we use our long homology guides to insert the transgene at a precise site in the genome that is expressed under the control of a potent endogenous promoter, like the albumin promoter. By not using exogenous promoters to drive expression of our transgene, we avoid the potential for off-target integration of promoters, which has been associated with an increased risk of cancer. We believe our choice of strong endogenous promoters will allow us to reach therapeutic levels of protein expression from the transgene with the modest integration rates typical of the highly accurate and reliable process of HR. We have observed the accurate insertion of the transgene and the resulting expression by the cells in animal models *in vivo* and human cells *in vitro*.
- **Nuclease-free genome editing.** By harnessing the naturally occurring process of HR, GeneRide is designed to avoid undesired side effects associated with exogenous nucleases used in conventional gene editing technologies. The use of these engineered enzymes has been associated with genotoxicity, including chromosomal alterations, resulting from the error-prone DNA repair of double-stranded DNA cuts. Avoiding the use of nucleases also reduces the number of exogenous components needed to be delivered to the cell.
- **Modularity.** We believe our modular approach will allow GeneRide to deliver robust, tissue-specific gene expression that will be reproducible across different therapeutics targeting the same tissue. The AAV capsid serves as the vehicle that enables delivery of the rest of the components to cells in the body. We and our research partners have done extensive work in developing vectors designed to be highly efficient in delivering their contents to specific target tissues such as the liver. The homology guides, which are independent of the transgene, are segments of DNA that each are hundreds of bases long and direct the integration of the target gene to a precise location in the genome. This location is critical because it determines which endogenous promoter will express the transgene. By substituting a different transgene within the GeneRide construct, we believe we can deliver that transgene to address a new therapeutic indication while substantially maintaining all other components of the construct. We believe, for example, that a new therapy based on liver expression of a transgene could use the same capsid and homology guides as LB-001 with the transgene for the new therapy replacing the *MUT* gene from LB-001. We expect this approach will allow us to leverage common manufacturing processes and analytics across our future GeneRide product candidates and could potentially shorten the development process of future programs.

LB-001 for the Treatment of Methylmalonic Acidemia (MMA)

We are developing our product candidate, LB-001, for the treatment of MMA. LB-001 contains a transgene coding for *MUT*, the most common gene deficiency in patients with MMA. LB-001 is designed to target liver cells and insert the *MUT* transgene into the albumin locus. We plan to advance LB-001 to an IND filing by the end of 2019 and into a Phase 1/2 clinical trial in pediatric MMA patients in 2020.

MMA Disease Background

MMA can be caused by mutations in several genes which encode enzymes responsible for the normal metabolism of certain amino acids. The most common mutations are in the gene for *MUT*, which cause complete or partial deficiencies in its activity. As a result, a substance called methylmalonic acid and other potentially toxic compounds can accumulate, causing the signs and symptoms of MMA. The following figure illustrates the effect of *MUT* deficiency in liver cells.

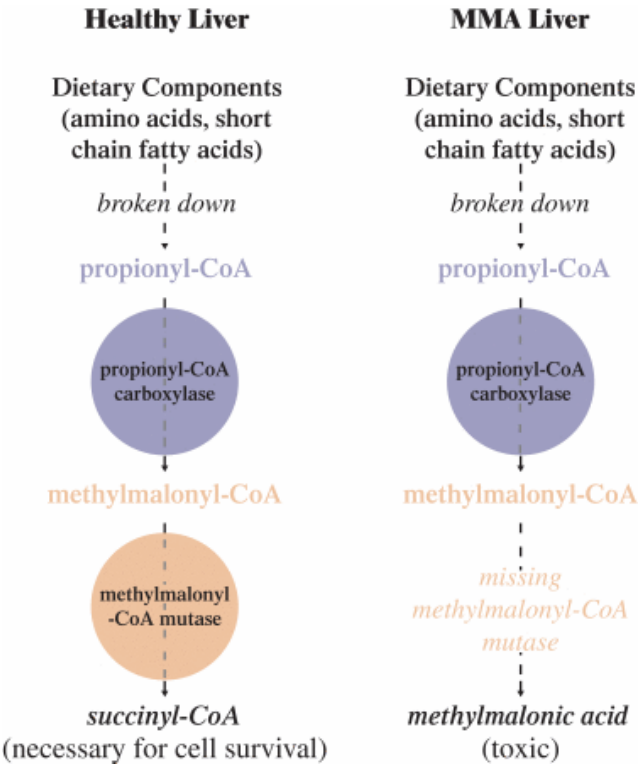


Figure 6. Mutations in *MUT* result in a disorder of the metabolic pathway for branched chain amino acids, specifically methionine, threonine, valine and isoleucine.

The effects of MMA usually appear in early infancy, with symptoms including lethargy, vomiting, dehydration and failure to thrive. Patients with MMA have long-term complications including feeding problems, intellectual disability, kidney disease and pancreatitis. Without treatment, MMA leads to coma and death. There are currently no approved therapies for MMA and the outlook for MMA patients remains poor. Management of the disease is limited to a low-protein, high-calorie diet, lacking amino acids normally processed by the *MUT*

pathway. Despite dietary management and vigilant care, MMA patients, especially those with the most severe deficiencies in *MUT*, often suffer neurologic and kidney damage exacerbated during periods of catabolic stress when injury, infection or illness trigger the breakdown of protein in the body. Life expectancy for patients with MMA has increased over the past few decades, but is still estimated to be limited to approximately 20 to 30 years. Quality of life for both patients and their families and caregivers is significantly impacted by the disease due to the constraints it places on school life and social functioning. Early intervention in this vulnerable population is essential to combat the manifestation of irreversible clinical disease pathologies.

The incidence of MMA in the United States is reported to be 1 in 50,000 births, with a current prevalence of approximately 1,600 to 2,400 patients in the United States. The proportion of MMA patients with the *Mut* mutation is estimated at approximately 63% of the total MMA population. We estimate the number of MMA patients with the genetic deficiency targeted by LB-001 to be 3,400 to 5,100 patients in key global markets, of which 1,000 to 1,500 patients are in the United States.

Over time, patients with MMA typically develop end-stage renal disease requiring kidney transplantation in adolescence. Combined liver-kidney transplantation, or early liver transplantation, has emerged as an intervention aimed at improving metabolic control. However, the finite number of liver donors, significant risks associated with surgery, high procedural costs (in the United States, approximately $740,000 on average for liver transplantation and $1.2 million on average for combined liver and kidney transplantation) and lifetime dependence on immunosuppressive drugs limit the widespread implementation of liver transplantation in patients with MMA.

Since *MUT* is a mitochondrial enzyme, we believe deficiencies in *MUT* cannot be corrected by enzyme replacement therapy in which functional enzyme is infused into the bloodstream. The most efficient way to get *MUT* enzyme inside the cell is to have it synthesized there. Several different approaches have been explored in animal models to accomplish this, including introducing mRNA to encode *MUT* directly into cells or introducing the gene for *MUT* into cells using a viral vector. While both of these approaches help to validate that the introduction of a functional *MUT* gene can ameliorate symptoms, they also each have a key limitation in that the therapeutic benefit is transient. In the case of mRNA therapy, weekly intravenous administration of the *MUT* mRNA was required to maintain therapeutic levels of *MUT*, but it is not clear how frequently this therapy would need to be administered in patients. In the case of *MUT* gene therapy, the levels of *MUT* decreased over time. Without a treatment that is durable, multiple doses would be required. However, the patient's development of neutralizing antibodies to the viral vector used to deliver the *MUT* gene therapy limits the ability to administer subsequent doses. In addition, administration of an AAV vector bearing a strong exogenous promoter has been correlated with hepatocellular carcinoma following neonatal delivery.

We believe that introduction of a functional copy of the *MUT* gene into the genome of MMA patients would represent a much better approach, potentially providing lifelong therapeutic benefit from a single administration.

Our Solution—LB-001

LB-001 is our initial GeneRide product candidate, which we are developing for the treatment of MMA. LB-001 consists of a DNA construct including a gene encoding the human *MUT* enzyme encapsulated in an AAV capsid. The *MUT* enzyme coding sequence is coupled to the 2A peptide sequence and surrounded by homology guides that drive the integration of the *MUT* gene and the 2A peptide sequence into the chromosomal locus for the albumin gene. Based on the way our construct integrates into the albumin locus, the *MUT* gene is then expressed resulting in synthesis of *MUT* enzyme as a separate protein from albumin. We chose LK03, the AAV capsid we use in LB-001, because it has been optimized to target human liver cells.

The following graphic illustrates the GeneRide construct for LB-001 inside the LK03 AAV capsid.

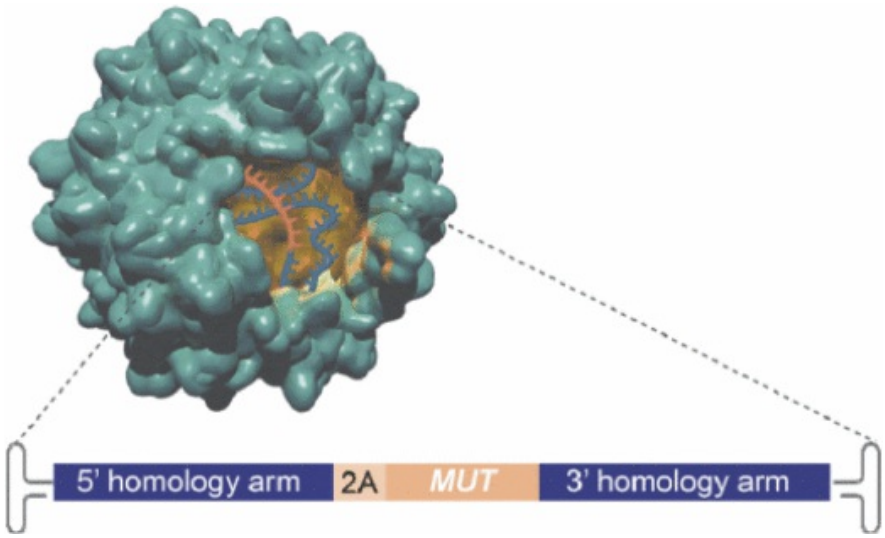


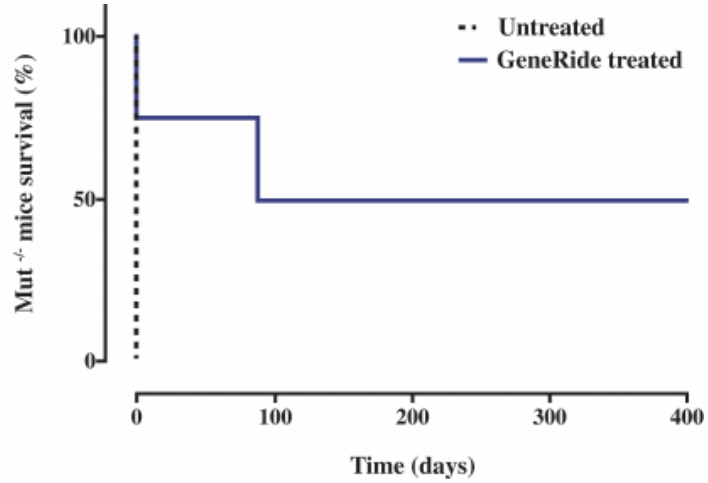
Figure 7. Structure of LB-001 GeneRide construct inside the LK03 AAV capsid.

Preclinical Data

Preclinical data for LB-001 was generated in two mouse models of MMA. In the first model, the gene for Mut had been rendered completely non-functional. This non-functional form of Mut is referred to as Mut-/-. Mice bearing this non-functional gene are believed to have a more severe deficiency than seen in the most severe cases of MMA in patients. Left untreated, these mice die within the first few days of life. A single intraperitoneal injection of a murine GeneRide construct of LB-001 into four neonatal mice resulted in increased survival for three out of four

mice, with two mice living for more than one year, as shown in the top panel of the following figure. In addition, these mice gained weight, when feeding freely, as shown in the bottom panel of the following figure.

Kaplan-Meier survival curves of *Mut* -/- mice treated with a GeneRide construct



Weight of *Mut* -/- mice over time

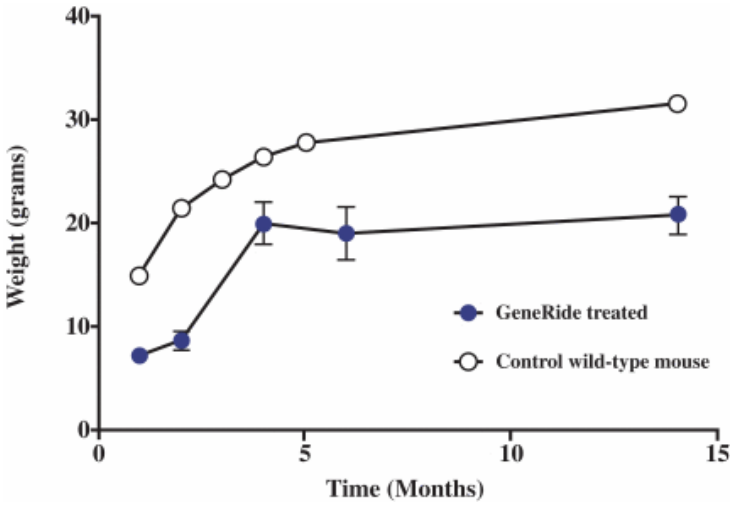


Figure 8. Mut-/- mice display enhanced survival (upper panel) and weight gain (lower panel) following neonatal treatment with a murine GeneRide construct of LB-001. Error bars indicate standard error of the mean, or SEM. Control mice were not included as a head-to-head comparator in our study; control mouse data is derived from studies completed by others.

The second mouse model of MMA, called MCK-Mut, is a modification of the Mut$^{-/-}$ mouse in which a functional copy of the mouse Mut gene is placed under the control of the creatine kinase promoter. This allows Mut expression in muscle cells, which in turn allows mice to survive longer while still exhibiting many of the phenotypic changes seen in MMA patients. Five neonatal MCK-Mut mice received single injections of a murine GeneRide construct of LB-001. Expression of Mut was observed in these mice. At one month of age, these mice had significant improvements in weight gain compared to untreated MCK-Mut mice, as shown in the following figure. These results were statistically significant. P-value is a standard measure of statistical significance, with p-values less than 0.05, representing less than a one-in-twenty chance that the results were obtained by chance, usually being deemed statistically significant.

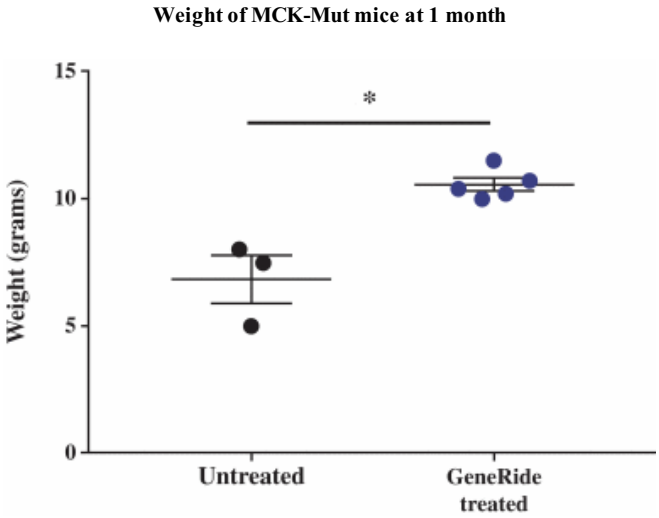


Figure 9. MCK-Mut mice treated with a murine GeneRide construct of LB-001 show significant improvement in growth at one month following a neonatal administration. * indicates p-value <0.05

GeneRide-treated MCK-Mut mice also had significant reductions in plasma levels of methylcitrate and methylmalonic acid, disease-relevant toxic metabolites and diagnostic biomarkers that accumulate in patients with MMA, as shown in the following figure.

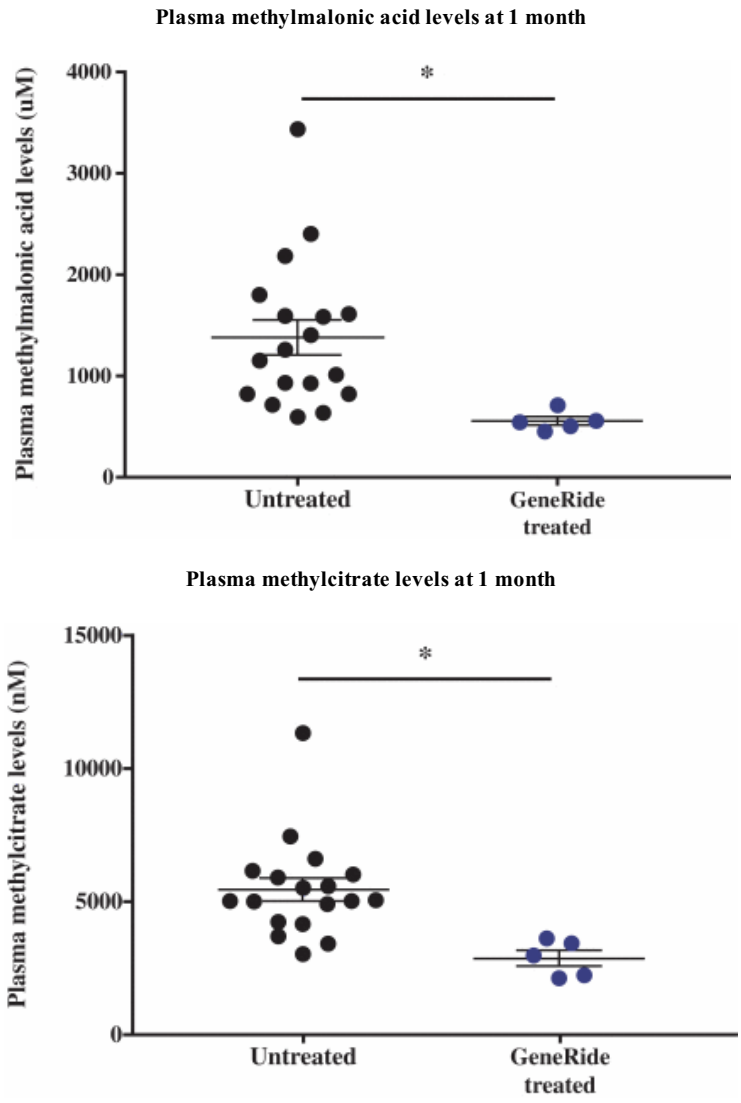


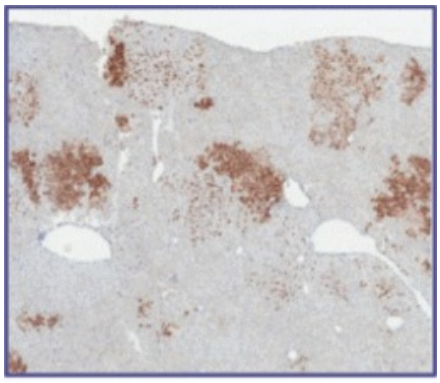
Figure 10. MCK-Mut mice treated with a murine GeneRide construct of LB-001 show significant reduction of two circulating disease related metabolites at one month, following a neonatal administration. Upper panel shows the reduction in plasma methylmalonic acid concentrations. Lower panel shows the reduction in plasma methylcitrate concentrations. Not all untreated mice were included as a head-to-head comparator. Untreated mouse data includes historical control mice. * indicates p-value <0.05

One of the limitations of AAV-directed HR gene editing has been the relatively modest rates of chromosomal integration. We address this limitation in our LB-001 program in multiple ways. First, we make use of an AAV capsid, LK03, which has been optimized to target human liver cells. Second, we target genomic insertion into the locus for the albumin gene. Albumin is the most highly expressed protein in the liver and normal expression of most other proteins is only a fraction of that of albumin. Even a modest integration rate may, therefore, express therapeutic levels of protein. Transcriptionally active genes, of which albumin is one, are more susceptible to transgene integration using HR.

Third, the presence of a functional *Mut* enzyme itself has been observed to provide a selective advantage to hepatocytes over those lacking *Mut*. Over time, this selective advantage leads to an increased proportion of liver cells that contain the functional copy of *Mut*. This can be observed in an experiment we conducted in mice in which a murine GeneRide construct was introduced into mice with and without a functioning copy of *Mut* in the liver. The initial GeneRide integration frequencies in both sets of mice were less than 4%. Over time, the number of modified cells remained the same in mice that naturally express *Mut* in the liver (Mut+/- in liver). However, after more than one year, in the mice genetically deficient in liver *Mut* (*Mut*-/- in liver), the percent of cells expressing *Mut* increased to 24% as shown in figure 11. This selective advantage could be attributed to improvements in mitochondrial function as a result of *Mut* expression and restoration of the deficient amino acid metabolic pathway.

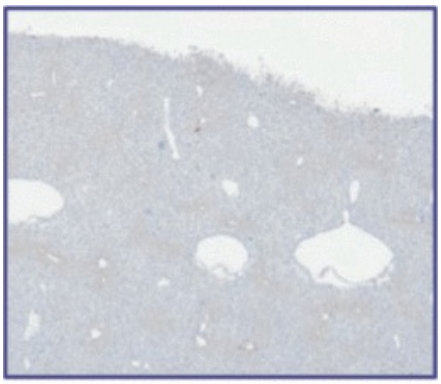
RNAscope analysis of liver sections following treatment with a GeneRide construct

Treatment of mouse deficient in liver *Mut* with a GeneRide construct



GeneRide delivered *Mut* expressed 24% of hepatocytes

Treatment of mouse expressing *Mut* in liver with a GeneRide construct



GeneRide delivered *Mut* expressed 3% of hepatocytes

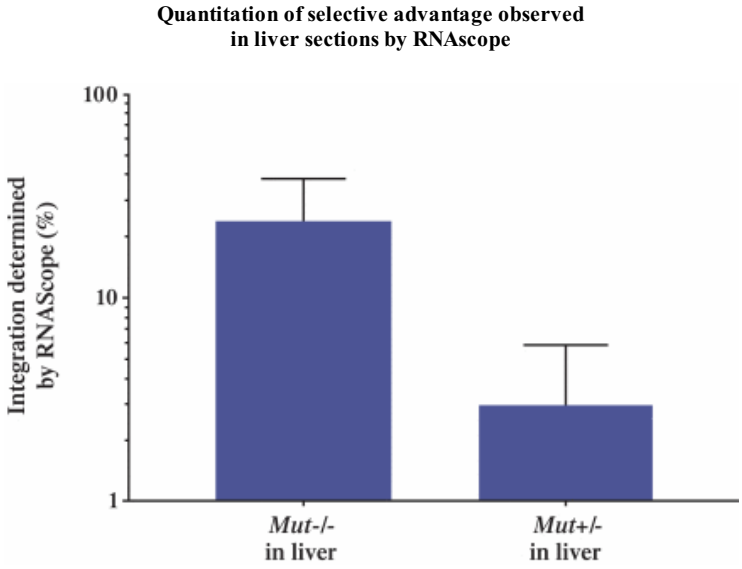


Figure 11. Treatment with GeneRide can result in a selective advantage to modified liver cells. Upper panel: RNAscope analysis of liver sections from mice treated with a murine GeneRide construct of LB-001. Mice genetically engineered without (left) and with (right) a functioning copy of *Mut* in the liver were treated neonatally. After more than one year, cells expressing the *Mut* mRNA specific to our GeneRide construct (dark staining regions) were increased in the mice lacking a natural functioning copy of *Mut* in the liver, suggestive of a beneficial selective advantage of our GeneRide construct of LB-001. Lower panel: quantitation of RNAscope sections conducted by an independent pathologist.

Additional supporting evidence for selective advantage in these mice includes (i) quantification of cells with the *Mut* gene integrated at the albumin locus by an orthogonal long-range quantitative polymerase chain reaction, or LR-qPCR, as shown in Figure 12, lower panel, and (ii) detection of an increased rate of integration at the albumin locus by LR-qPCR at more than one-year compared to one month post dose, as shown in Figure 13.

Quantitation of selective advantage observed in liver sections by DNA integration assay

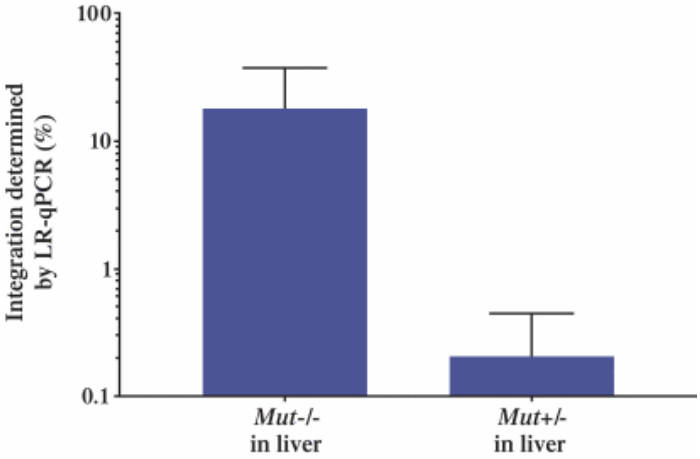


Figure 12. Percent of liver cells containing an integrated copy of the GeneRide specific *Mut* gene more than one year after a single neonatal administration of a *Mut* GeneRide construct in mice. LR-qPCR quantitation of DNA with the *Mut* gene integrated at the albumin locus. Error bars indicate SEM. LR-qPCR=long-range quantitative PCR.

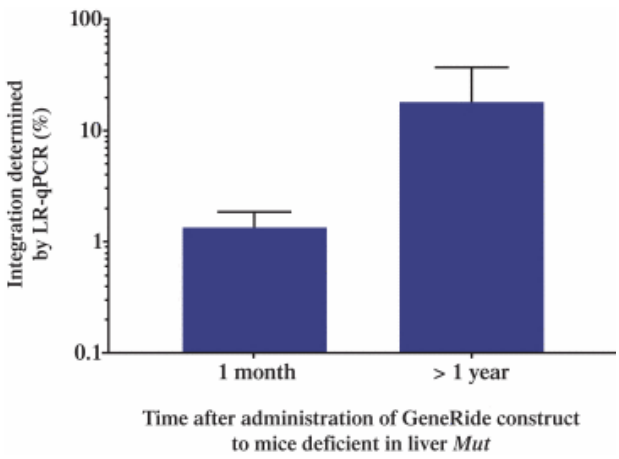


Figure 13. Increase in cells with integrated GeneRide construct observed over time. Mice deficient in liver *Mut* were administered a GeneRide construct as neonates. DNA analysis for integration at the albumin locus was conducted by LR-qPCR at 1 month and more than one-year post dose. Error bars indicate SEM.

In contrast to conventional AAV gene therapy approaches, in which the percentage of cells containing the therapy decreases over time as cells replicate and lose the virally encoded transgene, in the MMA mouse study, the percentage of cells containing a *Mut* GeneRide construct increased over time. These results support our belief that a single administration may provide lifelong benefits.

Future Product Opportunities

Future Liver-Directed Therapies

We expect that our initial product candidates, like LB-001, will be liver-directed therapies. The specificity of our candidates for the liver is determined both by the AAV capsid used and by the location of integration into the host cell's DNA. LB-001 utilizes the AAV capsid, LK03, which was designed to be highly efficient for transduction of human liver and is being evaluated in a gene therapy clinical trial in the United States conducted by another company. We chose to insert the transgenes for our liver-directed candidates into the albumin gene locus, which is only produced at a meaningful level in the liver, where it is the most highly expressed gene. We believe that the choice of albumin enhances our liver specificity because the active transcription enhances the rate of homologous recombination and the tissue-specific expression of the albumin gene will drive production of our transgene in the liver.

Using Liver as In Vivo Protein Factory

The liver is a major secretory organ that produces many proteins found in circulation. We believe this attribute can allow hepatocytes to deliver key therapeutic proteins to patients with genetic deficiencies. For example, we have demonstrated proof of concept in an animal model of hemophilia B using a murine GeneRide construct of LB-101, encoding human coagulation factor IX to correct a clotting deficiency. In this model, expression of human coagulation factor IX and blood coagulation was restored to normal levels after a single treatment in neonatal and adult diseased mice.

In addition, stable and therapeutic levels of human factor IX persisted for 20 weeks in neonatal wild type mice following administration of a murine GeneRide construct of LB-101, even after partial hepatectomy, or, PH, as shown in Figure 14. PH is a procedure where two-thirds of the liver is removed to trigger regenerative organ growth. With conventional AAV gene therapy, transgene expression following PH is drastically reduced.

Therapeutic and stable levels of human factor IX in plasma following treatment with a murine GeneRide construct of LB-101

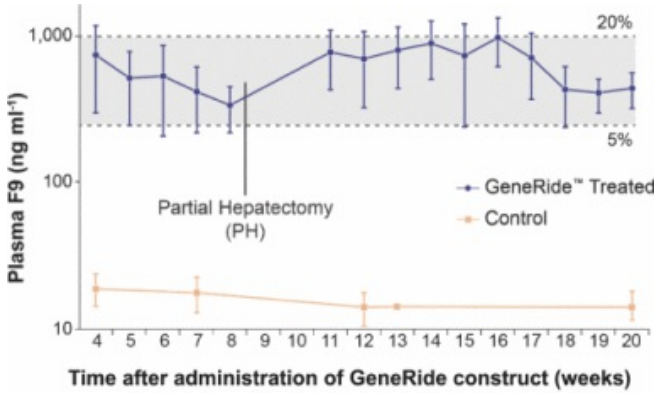


Figure 14. Therapeutic and stable levels of human factor IX with a murine GeneRide construct of LB-101. Stable and therapeutic levels of factor IX production from the liver, following neonatal administration, persisted for 20 weeks after administration, even with a PH conducted at 8 weeks of age (therapeutic levels of factor IX between 5% and 20% of normal factor IX shown by dashed lines and the shaded region). Error bars indicate standard deviation.

Inborn Errors of Metabolism

The liver is a key organ responsible for many metabolic and detoxifying processes. Dozens of monogenic diseases, including MMA, arise from deficiencies in liver enzymes involved in metabolic pathways. We have generated additional proof of concept data in animal models to address another rare inborn error of metabolism, Crigler-Najjar syndrome. Patients with Crigler-Najjar are unable to metabolize and remove bilirubin from circulation, resulting in lifelong risk of neurological damage and death. A murine GeneRide construct of LB-301, with the gene for bilirubin uridine diphosphate glucuronosyl transferase, or UGT1A1, as the transgene, was used to correct the gene deficiency in an animal model of Crigler-Najjar syndrome. The introduction of UGT1A1 into the albumin locus in mouse liver cells resulted in normalization of bilirubin levels and long-term survival of mice deficient in UGT1A1 from less than twenty days to at least one year, as shown in figure 15. Additional

indications we may pursue in this category include phenylketonuria, ornithine transcarbamylase deficiency and glycogen storage disease type 1A.

12 month survival after treatment with GeneRide construct in Crigler-Najjar syndrome mouse model

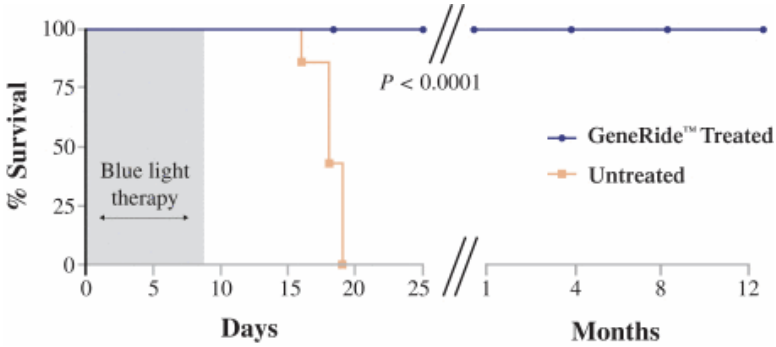


Figure 15. Increased survival in a mouse model of Crigler-Najjar syndrome following neonatal administration of a GeneRide construct delivering UGT1A1. Untreated animals (n=6) all died within 20 days of birth without continued blue-light therapy. Blue-light therapy, a treatment that facilitates clearance and reduction of toxic bilirubin levels, was applied from birth to Day 8. Without continued blue-light therapy, animals treated with a GeneRide construct (n=5) survived for one year.

Multi-Organ Diseases

Some genetic mutations result in both protein deficiencies and over-expression of deleterious proteins, leading to pathogenesis. One such disease is A1ATD. In A1ATD, patients have a deficit of circulating A1AT and can develop severe liver damage, which may necessitate a liver transplant. This is because AATD is a dominant negative genetic disease, in which the defective copy of the gene is associated with symptoms even in the presence of a normal copy. AATD is another genetic disease that has been corrected in a mouse model using a murine GeneRide construct of LB-201. The GeneRide construct used in the mouse model included a normal copy of the gene as well as a microRNA that was designed to reduce the expression of the deleterious gene. Expression of the transgene and downregulation of the mutant gene were evident in these mice for at least eight months.

Discovery Engine

We intend to choose a clinical development candidate from among these programs or from one of our other internal programs by the end of 2019. The key criteria we use in selecting development programs is unmet clinical need, the requirement to intervene early, well-understood biology, existing animal disease model, the ability to rapidly generate clinical proof of concept data and technical feasibility. We will also prioritize indications where we believe restoration of a modest level of transgene expression can provide a therapeutic benefit and where selective advantage of modified hepatocytes may further increase the proportion of corrected cells in the tissue over time. Our initial focus will be on hepatic and systemic diseases where liver-directed therapy is likely to provide therapeutic benefit. We expect that later product candidates will include products that target other tissues such as the CNS or muscle.

Continued Evolution of the GeneRide Platform

We continue to work to optimize key aspects of our platform from the design of the constructs and capsids to manufacturing at a commercial scale.

- **AAV capsid.** AAV capsids are designed to be highly efficient in delivering their contents to specific target tissues such as the liver. Extensive work has been done by our founders to identify capsids better suited for clinical use in the liver and other indications. For example, LK03, the AAV capsid we licensed from the Kay Lab at Stanford and use in LB-001, was developed to be liver selective. A recently published study found that the prevalence of neutralizing antibodies against LK03 is low in general (23%), particularly in late childhood, which we believe makes this capsid especially suitable for AAV gene therapy in pediatric patients. LK03 is also currently being used by other companies to treat hemophilia patients with liver selective gene therapy. In addition, we have recently licensed additional capsids from the Kay Lab and entered a partnership with CMRI to develop next generation viral vectors.
- **Homology guides and integration sites.** Our genome editing technology has the potential advantage that the homology guides and integration sites for one therapy can be applied to other therapies that target the same tissue. We intend to apply the knowledge we gain through the optimization of the rate of homologous recombination and gene expression levels to subsequent product candidates.
- **Targets.** We continue to evaluate a broad range of potential targets, starting with those that correspond to genes normally expressed in the liver, continuing to other tissues related to liver expression, and finally to considering targets that are best addressed directly in other tissues such as the CNS or muscle.
- **Selection.** A potential advantage of our genome editing technology is its durable nature arising from chromosomal integration. We have identified therapies where correction of a gene deficiency may provide a selective advantage to cells and drive expansion of the percentage of cells containing the transgene. We and our collaborators are also assessing methods of providing a selective advantage to treated cells even when the transgene does not provide a selection advantage at the cellular level. One such method involves adding an element to a GeneRide construct such that cells that do not incorporate the element are at a selective disadvantage when patients are treated with an external agent. We believe that these and related methods will enable us to enrich the number of cells containing the desired gene ensuring that patients derive long-term therapeutic benefit.

Manufacturing

We believe we are well-positioned to drive the continued development of our GeneRide technology for the treatment of severe genetic diseases. We have assembled extensive expertise in capsid development, AAV vector design, product development and manufacturing, as well as a broad intellectual property estate, an experienced management team and a world-class group of scientific advisors and network of leading contract development and manufacturing organizations and academic collaborators.

Additionally, we are developing an AAV vector manufacturing process technology that we believe will be both reproducible and scalable. We believe that our work and advancements in viral vector design, capsid development and related manufacturing processes will serve as a strong foundation for the industrialization of our genome editing technology and ultimately enable us to realize the full potential of our GeneRide technology and our products on a commercial scale.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy, gene editing and genome editing fields, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience

and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization. Not only must we compete with other companies that are focused on gene therapy, gene editing and/or genome editing technologies, any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that utilize technologies encompassing genomic medicines to create therapies, including gene therapy and gene editing. There are additional companies that are working to develop therapies in areas related to our research programs.

Our focus is the development of genetic medicines using our proprietary GeneRide technology. If our current programs are approved for the indications we are pursuing or contemplate we may pursue, they may compete with other products currently under development, including gene editing and gene therapy products. There are a number of companies developing nuclease-based gene editing technologies using CRISPR/Cas9, TALENs, meganucleases, Mega-TALs and ZFNs, including CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Sangamo Therapeutics and Precision BioSciences. We may also compete with companies developing gene therapy products, including Homology Medicines, Audentes Therapeutics, bluebird bio, uniQure and Voyager Therapeutics.

Any products we may develop could also face competition from other products approved to treat the same disease based on other types of therapies, such as small molecule, antibody or protein therapies. There are several companies developing competing products that target MMA, the indication for which we are developing LB-001. These companies include Moderna Therapeutics with an mRNA based approach, Selecta Biosciences with AAV gene therapy, and Hemoshear Therapeutics using a small molecule. While none of these companies have clinical-stage programs for these therapies, any of them may obtain regulatory approval for a treatment for MMA before LB-001, which could negatively affect our ability to successfully commercialize LB-001, if approved.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or 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 more rapidly 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. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience and availability of reimbursement.

Furthermore, we rely upon a combination of patents and trade secret protection, as well as license and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to LB-001 and any future product candidates. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement. If, therefore, we are unable to obtain and maintain patent

protection for our technology and products or if the scope of the patent protection obtained or in-licensed is not sufficiently broad or if the validity of such patent is threatened, we may not be able to compete effectively in our markets, as it could create opportunities for competitors to enter the market or dissuade other companies from collaborating with us to develop products and technology, any of which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved. For more information regarding these competitive risks, see "Risk Factors—Risks Related to Commercialization."

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. We seek to protect our proprietary position by, among other things, exclusively licensing and filing U.S. and certain foreign patent applications related to our platform technology, existing and planned programs, and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation, and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We additionally rely on regulatory protection afforded through orphan drug designations, data exclusivity, market exclusivity, and patent term extensions where available.

Our in-licensed patents and patent applications are directed to various aspects of our gene insertion and gene targeting technologies, including technology applied to treatment of human diseases by targeted insertion and expression of therapeutic transgenes and viral vector technology for transgene delivery. The licenses are, in some cases, limited to certain technical fields and/or therapeutic indications. We intend to pursue, when possible, additional patent protection, including filing patent applications seeking to protect composition of matter, method of use, and process claims, directed to our product development programs. We also intend to pursue rights to existing technologies through one or more licenses from third parties.

Notwithstanding these efforts, we cannot be sure that patents will be granted with respect to any patent applications we have licensed or may license or file in the future, and we cannot be sure that any patents we have licensed or patents that may be licensed or granted to us in the future will not be challenged, invalidated, or circumvented or that such patents will be commercially useful in protecting our technology. Moreover, trade secrets can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

For more information regarding the risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property."

Our intellectual property portfolio as of March 21, 2019 is summarized below. For some of our pending patent applications, prosecution has yet to commence. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO is often significantly narrowed by the time they issue, if they issue at all. We expect this to be the case with respect to our pending patent applications referred to below.

Nucleic Acid Delivery

We have non-exclusively licensed from The Board of Trustees of the Leland Stanford Junior University, or Stanford, two families of patents and patent applications, or Family 1 and Family 2, relating to AAV capsid polypeptides with improved properties useful for nucleic acid transfer applications and their manufacture and

methods of use. Family 1 includes four granted U.S. patents in the U.S. and one granted European patent. The issued U.S. patents in Family 1 are expected to expire in 2027. Patent term extensions could result in later expiration dates. Family 2 includes two granted U.S. patents and pending applications in the U.S., Europe, and Hong Kong. The issued U.S. patents in Family 2, and any which may later issue from a pending Family 2 patent application, are expected to expire in 2032. Patent term adjustments or patent term extensions could result in later expiration dates. For more information regarding the terms of our license to Family 1 and Family 2, please see "License Agreements."

Non-Disruptive Gene Targeting

We have exclusively licensed from Stanford and the Board of Regents of the University of Texas System, or UT, patent applications relating to technology for the insertion of a gene or genes of interest at a target genomic locus without disruption of endogenous gene expression, or Family 3. Family 3 includes one pending patent application in each of the U.S. and Europe. Any patent which may issue from a pending Family 3 patent application is expected to expire in 2033. Patent term adjustments or patent term extensions could result in later expiration dates. For more information regarding the terms of our license to Family 3, please see "License Agreements."

Genome Editing without Nucleases

We have exclusively licensed from Stanford patent applications relating to technology for the nuclease-free insertion of a gene or genes of interest at a target genomic locus without disruption of endogenous gene expression, or Family 4. Family 4 includes patent applications pending in eleven jurisdictions including the U.S., Europe, Canada, China, Korea, and Japan. Any patent which may issue from a pending Family 4 patent application is expected to expire in 2035. Patent term adjustments or patent term extensions could result in later expiration dates. For more information regarding the terms of our license to Family 4, please see "License Agreements."

AAV Capsids which Exhibit an Enhanced Neutralization Profile and/or Increased Transduction or Tropism in Human Liver Tissue or Hepatocyte Cells

We have non-exclusively licensed from Stanford patent applications, or Family 5, relating to recombinant AAV capsids resistant to pre-existing human neutralizing antibodies and/or characterized by increased transduction or tropism in human liver tissue or hepatocyte cells, useful for nucleic acid transfer applications and their manufacture and methods of use. Family 5 includes one granted U.S. patent and patent applications pending in six jurisdictions including the U.S., Europe, Australia, Canada, China and Japan. The issued U.S. patent in Family 5, and any patent which may issue from a pending Family 5 patent application is expected to expire in 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

Synthetic codon-optimized MUT gene

We have non-exclusively licensed from the U.S. Department of Health and Human Services, as represented by the National Human Genome Research Institute, an Institute of the National Institutes of Health (the "NIH"), patents and patent applications relating to synthetic polynucleotides encoding methylmalonyl-CoA mutase *(synMUT)* and exhibiting augmented expression in cell culture and/or in a subject. The *synMUT* license includes at least two granted U.S. patents, one granted European patent, and a pending application in the U.S. The issued U.S. patents under the *synMUT* license and any which may later issue from a pending patent application are expected to expire in 2034. Patent term adjustments or patent term extensions could result in later expiration dates. For more information regarding the terms of the *synMUT* license, please see "License Agreements

In addition to the above, we have also filed a U.S. Provisional application and a PCT application directed to non-disruptive gene therapy for the treatment of MMA.

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 U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by 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 product and other factors. There can be no assurance that any of our pending patent applications or the pending patent applications licensed to us will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents or the pending patent applications licensed to us.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims, if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents or patents that we license. Any issued patents that we may receive or license 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 U.S. that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a treatment method or product candidate we may develop, it is possible that, before any of our technology can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective technology and any competitive advantage such patent may provide.

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, by executing collaboration agreements containing confidentiality obligations with our collaborators, and agreements containing non-competition, non-solicitation, confidentiality, and invention assignment obligations with our employees and consultants, including our scientific advisors. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights.

Trademarks

Our registered trademark portfolio currently contains allowed trademarks in the United States for the marks LOGICBIO and GENERIDE.

License Agreements

We are a party to a number of license agreements under which we license patents, patent applications, and other intellectual property from third parties. The licensed intellectual property covers some of the compositions that we are researching and developing and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

The Board of Trustees of the Leland Stanford Junior University License Agreements

In December 2015, as amended in January 2018, we entered into a license agreement with Stanford pursuant to which we obtained an exclusive, worldwide license to make, have made, use, import, offer to sell and sell products covered by certain patent rights to the GeneRide technology owned by Stanford within certain fields of use.

This exclusive license grant is limited to the following fields: (a) human therapeutics to treat methylmalonic acidemia, propionic acidemia, HIV, influenza, malaria, Crigler-Najjar syndrome, Tyrosinemia Type I, Wilson's disease, hemophilia B, Glycogen Storage Disease 1 and Glycogen Storage Disease 3, and (b) the prevention, treatment or diagnosis via genome editing without a nuclease of certain additional indications with respect to liver tissue and certain other tissues to be nominated by us, subject to the terms of the agreement.

Pursuant to the Stanford license agreement, we also obtained (i) a non-exclusive license to make, have made, use, import, offer to sell and sell products covered by the foregoing GeneRide patent rights in the field of human therapeutics to treat hemophilia A (via genome editing without a nuclease) and Alpha-1 antitrypsin disease; (ii) a non-exclusive license to make, have made, use, import, offer to sell and sell products covered by certain patent rights with respect to AAV capsids owned by Stanford within the same fields of use that apply to the license under the patent rights to the GeneRide technology owned by Stanford; (iii) an exclusive license to make, have made, use, import, offer to sell and sell products covered by certain capsid-related patent rights owned by Stanford within the field of the diagnosis, prevention or treatment of phenylketonuria in humans; and (iv) a non-exclusive license to certain related know-how.

The license grant from Stanford under the patent rights to the GeneRide technology owned by Stanford does not extend to autologous *ex vivo* use for non-episomal DNA delivery and maintenance for hematopoietic stem cells for sickle cell or beta thalassemia.

The rights licensed to us are sublicensable through a single tier without Stanford's consent.

Under the terms of the agreement, as amended, we paid a one-time, non-refundable upfront fee of $75,000, issued Stanford 130,894 shares of our common stock, and subsequently issued 56,097 additional shares of common stock pursuant to Stanford's anti-dilution rights under the agreement. In addition, pursuant to its rights under the agreement, Stanford purchased shares of our Series A Preferred Stock and Series B Preferred Stock. We are required to pay Stanford low single-digit royalties on net sales of products as well as a portion of non-royalty sublicensing revenues. Our obligation to pay royalties will expire (i) on country-by-country basis with respect to net sales of any specified product sold, used, manufactured or imported in an applicable country until the expiration of the last valid claim within the licensed patents in such country covering such licensed product; and (ii) with respect to net sales of any such product, ten years from the first commercial sale of any licensed product. We are also obligated to pay annual maintenance fees, which are fully creditable against any royalty payments made by us, and up to an aggregate amount of $1.3 million of development milestone payments. We were also required to reimburse Stanford for all patent prosecution costs incurred prior to the agreement with respect to the patent rights to the GeneRide technology and for all future patent prosecution costs with respect to the patent rights to the GeneRide technology. We do not have the right to control patent prosecution with respect to the licensed patent applications, but we do have the first right to enforce any patents which may issue from these patent applications.

The term of the license agreement will continue so long as there is a valid claim of a licensed patent. Stanford may terminate the agreement upon at least 60 days' notice to us if (i) we are in material default in the provision of any report or payment of any amounts due to Stanford under the agreement, (ii) we do not use commercially reasonable efforts to develop or commercialize licensed products; (iii) we do not achieve certain diligence milestones within the mutually agreed timeline; (iv) we are in material breach of any provision of the agreement; or (v) provide any materially false report to Stanford. We may terminate the agreement at any time upon at least 30 days' notice to Stanford.

The Board of Regents of the University of Texas System License Agreement

In May 2018, we entered into a license agreement with the University of Texas, pursuant to which we obtained an exclusive, worldwide license to manufacture, have manufactured, distribute, have distributed, use, offer for sale, sell, lease, loan or import products covered by certain patent rights to the GeneRide technology owned by the University of Texas (jointly with Stanford) within certain fields of use.

This exclusive license grant is limited to the following fields: (a) human therapeutics to treat methylmalonic acidemia, propionic acidemia, HIV, influenza, malaria, Crigler-Najjar Syndrome, Tyrosinemia Type I, Wilson's disease, hemophilia B, Glycogen Storage Disease 1, Glycogen Storage Disease 3 and any other human disease of liver tissue that affects less than 200,000 persons in the United States as of the effective date of the agreement, and (b) the prevention, treatment or diagnosis via genome editing without a nuclease of certain additional indications with respect to certain tissues to be nominated by us, subject to the terms of the agreement.

Pursuant to the University of Texas license agreement, we also obtained a non-exclusive license to certain related know-how.

The rights licensed to us are sublicensable through multiple tiers without the consent of the University of Texas.

Under the terms of the agreement we paid a one-time, non-refundable upfront fee of $25,000. We are required to pay the University of Texas low single-digit royalties on all net sales of products as well as a portion of any sublicensing revenues. We are also obligated to pay annual maintenance fees, which are fully creditable against any royalty payments made by us, and certain development and sales milestone payments up to $3.0 million. We are also required to reimburse the University of Texas for all future patent prosecution costs on a pro rata basis with other licensees. We do not have the right to control patent prosecution with respect to the licensed patent applications, but we do have the first right to enforce any patents which may issue from these patent applications.

The term of the license agreement will continue on a country-by-country and product-by-product basis until the later of the expiration of the last-to-expire valid claim of a licensed patent that covers such product in such country and 10 years from the date of the first commercial sale of such product in such country. The University of Texas may terminate the agreement in its entirety or with respect to any applicable part of the licensed subject matter, field of use or licensed territory, or convert the exclusive license to a non-exclusive license, if (i) we fail to timely make a required payment to the University of Texas under the agreement; (ii) we are in material breach of a provision of the agreement and fail to timely cure such breach; (iii) we breach any payment obligation under the agreement three or more times in any 12-month period; (iv) we initiate, or an affiliate or sublicense initiates, a patent challenge against a licensed patent; or (v) we become bankrupt or insolvent, our board elects to liquidate our assets or dissolve the business, we cease business operations, we make an assignment to the benefit of our creditors, or our business or assets are otherwise placed in the hands of a receiver, assignee or trustee. We may terminate the agreement in its entirety or with respect to any applicable part of the licensed subject matter, field of use or licensed territory upon at least 30 days' notice to the University of Texas.

The NIH

In December 2018, we entered into a license agreement with the NIH, pursuant to which we obtained a non-exclusive, worldwide license under certain specified patent rights relating to a synthetic codon-optimized MUT gene that is incorporated into the LB-001 GeneRide construct, to exploit products and practice processes that are covered by the licensed patent rights in the field of research, development, manufacture and commercialization of pharmaceutical products for the treatment or prevention of MMA using gene therapy constructs in humans. We have the right to grant sublicenses under the license granted by the NIH, concurrently with licenses of its proprietary or other in-licensed intellectual property rights, with the NIH's prior consent, not

to be unreasonably withheld. The license grant is subject to typical statutory requirements and reserved rights as required under federal law and NIH requirements, including a requirement to manufacture substantially in the United States products used or sold in the United States that embody Licensed Products or are produced through the use of Licensed Processes.

Under the terms of the License Agreement, the NIH is entitled to receive an upfront payment of $25,000, and payments of up to an aggregate of $9.7 million upon the achievement of certain specified development, regulatory and sales-based benchmarks. The NIH is also entitled to receive running royalties on annual net sales of Licensed Products (subject to reductions for combination products that include Licensed Products), at certain low- to mid-single digit royalty rates, which rates vary based on the geographic market in which a sale occurs (subject to certain annual minimum royalty payments). The milestones and running royalties will be payable with respect to Licensed Products that are no longer covered by the licensed patent rights in a country, if the products are the subject of orphan drug exclusivity in the country. Additionally, if we receive a priority review voucher or a foreign equivalent for a Licensed Product, we have an obligation to pay to the NIH (a) a mid-single digit percentage of the sale price of the voucher, if we sell the priority review voucher, or (b) a low-single digit percentage of the fair market value of the voucher, if the we use the voucher to obtain regulatory approval of its product for an orphan indication or in the Licensed Field. The NIH is also entitled to receive a low-single digit percentage of upfront consideration that we receive for a sublicense of the rights licensed under the License Agreement and a low-single digit percentage of any consideration received for any assignment of the License Agreement by us.

Under the terms of the License Agreement, we have an obligation to use reasonable commercial efforts to make Licensed Products and Licensed Processes reasonably available in the United States following first commercial sale, make reasonable quantities of Licensed Products or materials produced through the use of Licensed Processes available to patient assistance programs and achieve certain diligence milestones.

Unless earlier terminated, the term of the License Agreement will continue until the last to expire of the licensed patent rights and any orphan drug exclusivity covering a Licensed Product in any jurisdiction. The NIH may terminate the License Agreement if we are in default in the performance of any material obligations under the License Agreement if the default has not been remedied within ninety days after the date of notice in writing of the default. In addition, the NIH may terminate or modify, at its option, the License Agreement, if the NIH determines, taking into account the normal course of commercial development programs conducted with sound and reasonable business practices and judgment, that we (i) have willfully made a false statement of, or willfully omitted, a material fact in the license application or in any report required by the License Agreement, (ii) have committed a material breach of a covenant or agreement contained in the License Agreement, (iii) are not keeping Licensed Products or Licensed Processes reasonably available to the public after first commercial sale, (iv) cannot reasonably satisfy unmet health and safety needs or (v) cannot reasonably justify a failure to comply with its domestic manufacturing requirements under the License Agreement. We have a unilateral right to terminate the License Agreement in any country or territory by giving the NIH sixty days' written notice.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, sale, distribution, post-approval monitoring and reporting, marketing and export and import of drug products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Government Regulation of Biological Products

In the United States, biological products, including gene therapy products, are subject to regulation by the U.S. Food and Drug Administration, or FDA, under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Products also are subject to other federal, state and local statutes and regulations. Each clinical study protocol for a gene therapy product must be reviewed by the FDA and, in some instances, the National Institute of Health, through its Recombinant DNA Advisory Committee, or RAC. FDA approval must be obtained before marketing of biological products.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. The FDA and NIH have published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents, including as recently as July 2018, related to, among other things, the overall gene therapy development process, preclinical assessment, observing subjects in gene therapy studies for delayed adverse events, potency testing, and chemistry, manufacturing and control information in an IND for gene therapy.

Ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

The process required by the FDA before a biological products may be marketed in the United States generally involves the following:

- completion of extensive preclinical studies and tests in accordance with applicable regulations, including Good Laboratory Practice, or GLP, regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical-trial related regulations to evaluate the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of preclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the biologic will be produced to assess compliance with good manufacturing practices, or cGMPs, to assure that the facilities, methods and controls used in product manufacture are adequate to preserve the biologic's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices, or GTPs, for the use of human cellular and tissue products;
- potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the BLA;

- payment of user fees for FDA review of the BLA (unless a fee waiver applies); and
- FDA review and approval of the BLA, including satisfactory completion of an FDA advisory committee review, if applicable, prior to any commercial marketing or sale of the product in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our investigational medicines and any future investigational medicines will be granted on a timely basis, or at all.

Preclinical Studies

Before testing any biological product candidate, including our product candidates, in humans, the product candidate must undergo rigorous preclinical testing. The preclinical development stage generally involves laboratory evaluations of the chemistry, formulation and stability of the product candidate, as well as trials to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP regulations.

The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but the RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA also may impose clinical holds on a biological product candidate at any time before or during clinical studies due to safety concerns or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by, or under control of, the trial sponsor, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about most clinical trials must be submitted within specific timeframes for publication on the *www.clinicaltrials.gov* website.

There are additional requirements when a gene therapy study is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research. In those situations, prior to the submission of an IND to

the FDA, a protocol and related documentation must be submitted to and the study must be registered with the NIH Office of Science Policy, or OSP, pursuant to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA; however, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH is responsible for convening the RAC, a federal advisory committee that discusses protocols that raise novel or particularly important scientific, safety or ethical considerations, at one of its quarterly public meetings. The OSP will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OSP website and may be accessed by the public.

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

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a larger number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Annual progress reports detailing the results of the clinical studies must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor, acting on its own or based on a recommendation from the sponsor's data safety monitoring board may suspend a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Human gene therapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period,

the number of patients the FDA will require to be enrolled in the studies in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these studies will be acceptable to the FDA to support marketing approval. The NIH has a publicly accessible database, the Genetic Modification Clinical Research Information System which includes information on gene transfer studies and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these studies.

Concurrently with clinical trials, companies usually complete additional preclinical studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Review and Approval

After the successful completion of clinical studies of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological products. The BLA must include results of the preclinical studies and clinical trials, detailed information relating to the product's chemistry, manufacture, controls, proposed labeling and other relevant information. The BLA must contain proof of safety, purity, potency and efficacy and may include both negative and ambiguous results of preclinical studies and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial application user fee, although the fee may be waived under certain circumstances. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original BLAs, the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. This review typically takes twelve months from the date the BLA is submitted to the FDA because the FDA has approximately two months to make a filing decision. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes

clinicians and other experts, for review, evaluation and 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. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with CGMP requirements and adequate to assure consistent production of the product within required specifications. For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with GTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical studies were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, GTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA ultimately may decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If the FDA issues a complete response letter, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical studies, sometimes referred to as Phase 4 clinical studies, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product in the United States. An applicant must request orphan drug designation before submitting a BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug

designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user fee waivers. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity. That means the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, by providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication; in the latter case, because health care professionals are free to prescribe products for off-label uses, the competitor's product could be used for the orphan indication despite our orphan exclusivity. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do of the same drug and same indication, as defined by the FDA, for which we are seeking, or if our product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If we pursue marketing approval for an indication broader than the orphan drug designation we have received, we may not be entitled to orphan drug exclusivity.

Expedited Development and Review Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs and biologics to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA also may review sections of the BLA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the BLA.

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

Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a

clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Once a BLA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if the FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. Under priority review, the FDA must review an application in six months, compared to ten months for a standard review. Most products that are eligible for fast track or breakthrough therapy designation also are likely to be considered appropriate to receive a priority review.

A biological product also can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including some regulatory exclusivity periods. This six-month exclusivity, which runs from the end of other exclusivity protection, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

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

Regenerative Medicine Advanced Therapies Designation

As part of the 21st Century Cures Act, enacted in December 2016, Congress amended the FDCA to facilitate an efficient development program for, and expedite review of regenerative medicine advanced therapies, which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Regenerative medicine advanced therapies, or RMAT, do not include those human cells, tissues, and cellular and tissue based products regulated solely under section 361 of the Public Health Service Act and 21 CFR Part 1271. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A drug sponsor may request that the FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. The FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy with RMAT designation that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence from clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Like the FDA's other expedited development programs, RMAT designation does not change the standards for approval but may expedite the development or approval process.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data that are adequate to assess the safety and efficacy of the product candidate for the claimed indications in all relevant

pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act, or FDASIA, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials or other clinical development programs.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials.

Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of conditions that violate these rules, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved BLA, including voluntary recall.

Once an approval or clearance of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards 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 mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

Biosimilars and Exclusivity

An abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Affordable Care Act. This amendment to the PHSA, in part, attempts to minimize duplicative testing. To date, the FDA has approved a number of biosimilars, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining its approach to reviewing and approving biosimilars.

Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, must be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Complexities associated with the larger, and often more complex, structure of biological products as compared to small molecule drugs, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. “First licensure” typically means the initial date the particular product at issue was licensed in the United States. One must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

The BPCIA is complex and only beginning to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other

aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA is subject to significant uncertainty.

Foreign Regulation

In order to market any product outside of the United States, we would need to 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 our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of other geographies, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively affect the regulatory process in others.

Other Healthcare Laws and Regulations

In addition to FDA restrictions on the marketing of pharmaceutical products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain approval. These laws include, but are not limited to the following:

- The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made under federally funded healthcare programs, such as Medicare and Medicaid. The term ‘‘remuneration’’ has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical and medical device manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other hand;
- The federal civil and criminal false claims laws, including, without limitation, the federal civil monetary penalties law and the civil False Claims Act, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment of federal funds, and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government. Actions under the civil False Claims Act may be brought by the Attorney General or as a *qui tam* action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program and creates federal criminal laws that prohibit 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 healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without the appropriate authorization by entities subject to

the law, such as healthcare providers, health plans, and healthcare clearinghouses and their respective business associates;

- The federal transparency requirements under the Physician Payments Sunshine Act, created under the Affordable Care Act, require certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to payments and other transfers of value provided to physicians and teaching hospitals and physician ownership and investment interests. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties;
- The Foreign Corrupt Practices Act, or the FCPA, prohibits any United States individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts;
- The FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- The U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product; and
- State and foreign equivalents of each of the healthcare fraud and abuse laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. We may also be subject to: state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that restrict payments that may be made to healthcare providers; state laws that require pharmaceutical manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state and local laws that require the registration of pharmaceutical sales representatives; and equivalent foreign laws and regulations. Further, we may be subject to state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Recent healthcare reform legislation has strengthened these federal and state healthcare laws. For example, the Affordable Care Act amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes to clarify that liability under these statutes does not require a person or entity to have actual knowledge of the statutes or a specific intent to violate them. Moreover, the Affordable Care Act provides that the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Violations of these laws can subject us to criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and

oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages and reputational harm, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our future operations and business.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any biological products for which we obtain regulatory approval. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded drug and biologic products. In the United States and markets in other countries, patients who are prescribed products generally rely on third party payors to reimburse all or part of the associated healthcare costs. Providers and patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. If approved, sales of our product candidates will depend, in part, on the availability of coverage and adequate reimbursement from third party payors. Third party payors include government authorities, managed care plans, private health insurers and other organizations.

In the United States, the process for determining whether a third party payor will provide coverage for a biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. With respect to biologics, 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 FDA approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost sharing obligation imposed on patients. A decision by a third party payor not to cover our product candidates could reduce physician utilization of a product. Moreover, a third party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third party reimbursement may not be available to enable a manufacturer to maintain price levels sufficient to realize an appropriate return on its investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third party payor's decision to cover a particular medical product does not ensure that other payors will also provide coverage for the medical product, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process usually requires manufacturers to provide scientific and clinical support for the use of their products to each payor separately and is a time consuming process.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide coverage and adequate reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. 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 we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Third party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning safety and efficacy. If third party payors do not consider a product to be cost effective compared to other available therapies, they may not cover that product after FDA approval or, if they do, the level of payment may not be sufficient to allow a manufacturer to sell its product at a profit.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the European Union, governments influence the price of products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those

products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert a commercial pressure on pricing within a country.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or the Affordable Care Act, was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; imposed a new federal excise tax on the sale of certain medical devices; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established the Center for Medicare and Medicaid Innovation at the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Some of the provisions of the Affordable Care Act have yet to be implemented, while certain provisions have been subject to legal and political challenges. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act. In December 2017, Congress repealed the tax penalty for an individual's failure to maintain Affordable Care Act-mandated health insurance as part of a tax reform bill. Further, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-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. Moreover, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress could consider additional legislation to repeal or replace elements of the Affordable Care Act, or adopt other healthcare reform measures. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation.

Other legislative changes have been adopted since the enactment of the Affordable Care Act. For example, the Budget Control Act of 2011 led to aggregate reductions of Medicare payments to providers of up to 2% per fiscal year that will remain in effect through 2027 unless additional Congressional action is taken. Further, on January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical 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. Further, the Trump administration released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. While some proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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.

We expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

Employees

As of December 31, 2018, we had 23 full time employees, including 16 with Ph.D. or other advanced degrees. Of these full time employees, 14 are engaged in research and development and 9 are engaged in general and administrative activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate and Other Information

LogicBio Therapeutics, Inc. was incorporated under the laws of the State of Delaware in August 2014. Our principal executive offices are located at 99 Erie St., Cambridge, Massachusetts 02139, and our telephone number is (617) 245-0399. Our website address is http://www.logicbio.com. The information contained on our website is not incorporated by reference into this Annual Report on Form 10-K, and you should not consider any information contained on, or that can be accessed through, our website as part of this Annual Report on Form 10-K.

We have three subsidiaries, LogicBio Therapeutics Research, LTD., a wholly owned Israeli subsidiary formed in January 2016, LogicBio Australia Pty Limited, a wholly owned Australian subsidiary formed in April 2018, and LogicBio Securities Corporation, a wholly owned Delaware subsidiary formed in December 2018. As of December 31, 2018, all operations had ceased for LogicBio Therapeutics Research, LTD.

You may read our Securities and Exchange Commission, or SEC, filings, including our proxy statements, annual reports 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 Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, over the internet at the SEC's website at *www.sec.gov*. We also maintain a website at *www.logicbio.com*, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report on Form 10-K.

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future. We may never achieve or maintain profitability.

We are a preclinical-stage genome editing company with a limited operating history. We have incurred net losses in each year since our inception, including a net loss of $17.6 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of approximately $27.2 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted most of our financial resources to research and development, including our preclinical development activities. We expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance LB-001, our lead product candidate, through preclinical and clinical development, expand our research and development capabilities and activities, develop new product candidates, initiate and complete clinical trials, seek regulatory approval and, if we receive approval from the U.S. Food and Drug Administration, or FDA, commercialize our product candidates. Our net losses may fluctuate significantly from quarter to quarter and year to year. Because of the numerous risks and uncertainties associated with genetic medicine product development, we are unable to accurately predict the timing or amount of increased expenses, when, if ever, we will generate revenue from the commercialization of products or whether we will achieve or maintain profitability. We anticipate that our expenses will also increase substantially if and as we:

- continue our current research programs and our preclinical development of any product candidates from our current research programs;
- initiate preclinical testing and clinical trials for LB-001 and any other product candidates we identify and develop;
- seek to identify, assess, acquire and/or develop additional research programs and additional product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- develop, optimize, scale and validate a manufacturing process and analytical methods for any product candidates we may develop;
- establish and build out internal process and analytical development capabilities and research and preclinical grade production;
- obtain market acceptance of any product candidates we may develop as viable treatment options;
- address competing technological and market developments;
- maintain, expand and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- further develop our GeneRide technology platform;
- hire additional technical, quality, regulatory, clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our process and product development, manufacturing and planned future commercialization efforts;

- make royalty, milestone or other payments under current or future in-license agreements;
- establish and maintain supply chain and manufacturing relationships with third parties that can provide adequate products and services, in both amount, timing and quality, to support clinical development and the market demand for any product candidate for which we obtain regulatory and marketing approval;
- lease and build new facilities, including offices and labs, to support organizational growth;
- validate and build-out a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- continue our transition operating as a public company.

Furthermore, our ability to successfully develop, commercialize and license our product candidates and potentially generate product revenue is subject to substantial additional risks and uncertainties. Each program and any product candidate we develop, will require additional preclinical and clinical development, potential regulatory approval in one or more jurisdictions, securing manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. See "—Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval" and "—Risks Related to Commercialization."

As a result of all of the above, as well as other potential factors, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. If we are unable to develop and commercialize one or more product candidates either alone or with collaborators, or if revenue from any product candidate that receives marketing approval is insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of any product candidates.

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize LB-001 and any other product candidate we may identify and develop. We will require additional capital, which we may seek to raise through equity offerings, debt financings, marketing and distribution arrangements, collaborations, strategic alliances, licensing arrangements or other sources, to enable us to complete the development and potential commercialization of LB-001 and any other product candidate. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts.

Based upon our current operating plan, we believe that our cash and cash equivalents as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements through 2020. We anticipate that we may need additional funding in order to complete the Phase 1/2 clinical trial of LB-001. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and activities associated with successful development of LB-001 and any other product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and, if applicable, any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the initiation, scope, progress, timing, costs and results of drug discovery, preclinical development, laboratory testing, and planned clinical trials for LB-001 and any other product candidates;

- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities, including resolving any potential clinical holds that may be imposed on us;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions;
- the achievement of milestones or occurrence of other developments that trigger payments under any of our current agreements or other agreements we may enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical or commercial-scale manufacturing activities;
- the costs of continuing to operate as a public company;
- the extent to which we in-license or acquire other products and technologies;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the cost of establishing sales, marketing and distribution capabilities for LB-001 and any other product candidates in regions where we choose to commercialize our product candidates, if approved; and
- the initiation, progress, timing and results of our commercialization of LB-001 and any other product candidates, if approved, for commercial sale.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that 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, even if we successfully identify and develop product candidates and one or more are approved, we may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of LB-001 or any other product candidates or potentially discontinue operations.

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

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific 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 additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate 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 never generated revenue from product sales and may never be profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. To date, we have not generated any revenue from our programs or any product candidate and do not anticipate generating revenues from product sales for the foreseeable future. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', ability to successfully:

- identify product candidates and complete research and preclinical and clinical development of any product candidates we may identify;
- obtain sufficient financial and other resources to complete the necessary preclinical studies and clinical trials of LB-001 and any other product candidate we may develop;
- obtain successful data from our clinical program that supports an acceptable risk-benefit profile of any product candidates in the intended populations;
- develop safe and effective delivery mechanisms for our in vivo therapeutic programs;
- achieve desirable medicinal properties for the intended indications;
- seek and obtain regulatory and marketing approvals for any product candidate for which we complete clinical trials;
- launch and commercialize any product candidate for which we obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualify for adequate healthcare coverage and reimbursement by government and third-party payors for any product candidate for which we obtain regulatory and marketing approval;
- develop, enhance, scale and validate a manufacturing process and analytical methods for any product candidates we may develop;
- implement effective strategies and knowledge management systems to ensure the integrity of data, specifically the completeness, consistency and accuracy of data used to ensure the safety, efficacy and quality of products manufactured;
- establish and maintain supply and manufacturing relationships with third parties that remain compliant with all relevant health authority and legal requirements and can provide adequate, in amount, timing and quality, products and services to support clinical development and the market demand for any product candidate for which we obtain regulatory and marketing approval;
- compete with other therapies and treatment options;
- obtain market acceptance of any product candidates we may develop as viable treatment options;
- obtain a positive recommendation from the Recombinant DNA Advisory Committee of the NIH;
- obtain a continued acceptable safety profile of the medicines following approval;
- address competing technological and market developments;
- implement internal systems and infrastructure, as needed;
- enter into collaborations to further the development of any product candidate;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintain, protect and expand our portfolio of intellectual property rights, including patents, trade secrets, know-how and non-patent exclusivity for our medicines;

- avoid and defend against third-party interference or infringement claims; and
- attract, hire and retain qualified personnel.

Additionally, because our technology involves genome editing, we are subject to additional challenges and risks that gene therapy companies face, including:

- regulatory requirements that govern gene and cell therapy products, which have changed frequently and may continue to change in the future, and few products that involve the genetic modification of patient cells have been approved in the United States or the European Union; and
- the FDA's recommendation of a follow-up observation period of up to 15 years or longer for all patients who receive treatment using genome editing therapies, necessitating us to adopt such an observation period for any product candidate we may develop.

Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval

We intend to identify and develop product candidates based on our novel GeneRide technology platform, which makes it difficult to predict the time and cost of product candidate development. No genome editing product has been approved in the United States or in Europe. There have only been a limited number of human clinical trials involving a gene editing product candidate and none of those trials has involved our nuclease-free genome editing technology.

We have concentrated our research and development efforts on product candidates utilizing our GeneRide technology. Our future success depends on the successful development of this novel therapeutic approach. To date, no product that utilizes our GeneRide technology has been approved. There have been a limited number of clinical trials of gene editing technologies, however no product candidates have been approved, and none of these clinical trials involved product candidates that utilize our GeneRide technology. In addition, because our programs are all in the research or preclinical stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any of our future product candidates that we cannot predict at this time. Any product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, results of tests of our product candidates in animal models for either safety or efficacy may not be predictive of results that may be observed in humans. Also, animal models may not exist for some of the diseases we expect to pursue. Our GeneRide genome editing approach harnesses homologous recombination, or HR, a naturally occurring DNA repair process that maintains the fidelity of the genome. The mechanism of action of this technology is still not completely understood. Therefore, it is and will be difficult for us to determine whether any of our product candidates will be able to properly integrate corrective DNA in or deliver gene transfer constructs to enough tissue cells to reach therapeutic levels. We cannot be certain that any of our product candidates will be able to meet safety and efficacy levels needed to be therapeutic in humans or that they will not cause significant adverse events or toxicities. 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 GeneRide technology platform, or any similar or competitive gene therapy or gene editing platforms, will result in the identification, development and regulatory approval of any medicines, or that other genetic medicine technologies will not be considered better or more attractive for the development of medicines. Any development problems we experience in the future related to our GeneRide technology platform or any of our research programs may cause significant delays or unanticipated costs, or we may not be able to solve for the issue. We may also experience delays in developing a capable and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or clinical trials that we may initiate or prevent us from commercializing any product candidates we may develop on a timely or profitable basis, if at all.

Because genome editing is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

Because genome editing is novel, the regulatory requirements governing any genome editing product candidates we develop are uncertain and subject to change. For example, the FDA recently issued several guidance documents regarding gene therapy in July 2018. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any genome editing product candidates we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy products, cell therapy products or products developed through the application of gene editing technology may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Furthermore, 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. As we are initially seeking 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 (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be 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, we may produce results that are 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. Other

regulatory authorities in the European Union and other countries, such as the CAT, may make similar comments with respect to these endpoints and data. Any product candidates 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. No genome editing product has been approved in the United States or in Europe.

Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research and development programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, increase the scope of process development, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

We have no history of conducting clinical trials or commercializing genetic medicine product candidates and we may encounter difficulties transitioning from a research-stage to clinical-stage company to ultimately a commercial-stage company, which may make it difficult to evaluate the prospects for our future viability.

We are an early-stage company. We were founded in 2014 and began operations in 2015. Our operations to date have been limited to financing and staffing our company, developing our technology, identifying and developing LB-001, undertaking preclinical studies, business planning and raising capital. All of our research programs are still in the preclinical or research stage of development, and the risk of failure in the biopharmaceutical industry for programs or products candidates at such stage of development is high. We have not yet demonstrated an ability to successfully initiate, conduct or complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approval, manufacture a clinical or commercial scale product or arrange for a third party to do so on our behalf or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes about six to ten years to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, but in many cases it may take longer. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing genetic medicine product candidates.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will eventually need to transition from a company with a research focus to a company capable of supporting clinical and, if any of our product candidates are approved, commercial activities. We may not be successful in such a transition.

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 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, if any, or if the outcome of our preclinical testing and studies will ultimately support the further development of any of our 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.

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 initiation of 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 obtain positive results from preclinical studies or initial clinical trials, we may not achieve the same success in future trials.

Clinical trials are expensive, difficult to design and implement, time-consuming and involve an uncertain outcome.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidates we may identify and develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans of any such product candidates. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and there is a high failure rate for product candidates proceeding through clinical trials. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biotechnology and genetic medicine industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of LB-001 for MMA or any other potential indication. Our future clinical trial results may not be successful.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates.

To date, we have not completed any clinical trials required for the approval of LB-001. Although we plan to advance LB-001 to an IND filing by the end of 2019 and into a Phase 1/2 clinical trial in 2020, we may experience delays in conducting any clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned to address clinical holds imposed by regulatory authorities or for other reasons, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;

- obtaining regulatory approval to commence a trial or to restart a trial following a clinical hold;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, approval at each site;
- recruiting suitable patients to participate in a trial;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- having patients complete a trial or return for post-treatment follow-up;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- clinical sites deviating from trial protocol or subjects dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- occurrence of serious adverse events associated with any product candidates we may develop that are viewed to outweigh their potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- difficulty in designing well-controlled clinical trials due to ethical considerations which may render it inappropriate to conduct a trial with a control arm that can be effectively compared to a treatment arm;
- difficulty in designing clinical trials and selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed 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 the product removed from the market after obtaining marketing approval;
- 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;
- be sued; or
- experience damage to our reputation.

We could encounter delays if a clinical trial is suspended or terminated by us, either independently or based on a recommendation by the Data Safety Monitoring Board, or DSMB, for such trial, by the IRBs of the institutions in which such trials are being conducted or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including (1) failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols; (2) inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold; (3) unforeseen safety issues or adverse side effects; (4) failure to demonstrate a benefit from using a drug; (5) changes in governmental regulations; or (6) administrative actions or lack of adequate funding to continue the clinical trial. Furthermore, we may rely on CROs and clinical trial sites to ensure the proper and timely conduct of clinical trials and while we would have agreements governing their committed activities, we would have limited influence over their actual performance, as described in "—Risks Related to Our Dependence on Third Parties."

Our lead product candidate, LB-001, is still in preclinical development. We plan to submit an IND for LB-001 in late-2019, and we cannot provide any assurance that the FDA will authorize us to initiate any of our planned clinical trials on a timely basis, or at all, or that the FDA will agree with the design of our protocol. LB-001 will

require extensive clinical testing before we are prepared to submit a biologic license application, or BLA, for regulatory approval. We cannot predict with any certainty if or when we might complete the development of LB-001 and submit a BLA for regulatory approval of LB-001 or whether any such BLA will be approved by the FDA. We may also seek feedback from the FDA or other regulatory authorities on our clinical development program, and the FDA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of LB-001 or any other product candidate we develop could be harmed. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials also ultimately may lead to the denial of regulatory approval of our product candidates.

Product development costs also will increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we may develop, could allow our competitors to bring products to market before we do and could impair our ability to successfully commercialize any product candidates we may develop, any of which may harm our business, financial condition, results of operations and prospects.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We or our collaborators may not be able to initiate or continue clinical trials for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. In addition, if patients are unwilling to participate in our genome editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy or genome editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products or for other reasons, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of any product candidates we may develop may be delayed.

We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. The enrollment of patients depends on many factors, including:

- the patient inclusion and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- severity of the disease under investigation;
- the proximity of patients to trial sites;
- the design of the trial;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;

- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion;
- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of genome editing as a therapeutic approach;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- inability to locate qualified local consultants, physicians and partners; and
- potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial sites.

Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop LB-001 or any other product candidates, or could render further development impossible.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we may develop, and any such approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if any product candidates we may develop meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a Risk Evaluation and

Mitigation Strategy, or REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop. Any of the foregoing scenarios could materially harm the commercial prospects for any product candidates we may develop and materially adversely affect our business, financial condition, results of operations and prospects.

Adverse public perception of genetic medicine, and gene editing in particular, may negatively impact regulatory approval of, or demand for, our potential products.

Our product candidates involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene editing and gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene editing are unsafe, unethical or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm and embryos. The Alliance for Regenerative Medicine in Washington has called for a voluntary moratorium on the use of gene editing technologies in research that involved altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene therapy or gene editing technologies, even if not ultimately attributable to product candidates we may discover and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, a decrease in demand for any such product candidates and a suspension or withdrawal of approval by regulatory authorities of our product candidates.

Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public

perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

We may not be successful in our efforts to identify additional product candidates.

Part of our strategy involves identifying novel product candidates. All of our product candidates are still in the preclinical or research stage of development. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is too complex and difficult to navigate successfully or economically.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify additional suitable product candidates for clinical development, this could harm our business, financial condition, results of operations and prospects.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

We currently have relationships with a limited number of suppliers for the manufacturing of our product candidates. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including data

management) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that can impact safety, efficacy and quality, and may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current good laboratory practices, or GLP, and cGMP regulations enforced by the FDA through its facilities inspection program. Some of our contract manufacturers have not produced a commercially-approved product and therefore have not yet obtained the requisite FDA approvals to do so. The facilities and quality systems of some or all of our third-party contractors, as well as any facilities and quality systems we may have in the future, must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

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

We have not evaluated any product candidates in human clinical trials. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. In the genomic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. There can be no assurance that our genome editing technologies will not cause undesirable side effects.

Serious adverse events or undesirable side effects caused by any product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities or unexpected characteristics, including death. A significant risk in many gene editing products is that the edit will be "off-target" (or "on-target," but unwanted) and cause serious adverse events, undesirable side effects, toxicities or unexpected characteristics. For example, off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. While we believe our GeneRide technology obviates this through the use of HR, we cannot be certain that off-target editing will not occur in any of our planned or future clinical trials. There is also the potential risk of delayed adverse events following exposure to gene editing therapy, due to the potential for persistent biological activity of the genetic material or other product components used to carry the genetic material. In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated.

If unacceptable side effects arise in the development of any of our product candidates, we, including in consultation with the DSMB, the FDA or the IRBs at the institutions in which our studies are conducted or DSMB, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. In that case, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would harm our business, financial condition, results of operations and prospects. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further clinical development of the product candidates. Treatment-related side effects also could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, the European Commission, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, which could harm our business, financial condition, results of operations and prospects.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient. A REMS may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or contraindication;
- we may be required to implement a REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, which could harm our business, financial condition, results of operations and prospects.

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

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved and 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 neither LB-001 nor any other product candidate we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of a BLA from the FDA. It is possible that the FDA may refuse to accept for substantive review any BLAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA-required studies, approval of any BLA or application that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully completes the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

We are heavily dependent on the success of LB-001, our lead product candidate, which is still under preclinical development, and if LB-001 does not receive regulatory approval in the United States or other jurisdictions, or is not successfully commercialized, our business will be harmed.

To date, we have invested a significant portion of our efforts and financial resources in the development of LB-001. Our future success and ability to generate product revenue is substantially dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize this product candidate. We currently have no products that are approved for commercial sale and may never be able to develop marketable products.

We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to LB-001. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of LB-001, which may never occur. We cannot be certain that LB-001 will be successful in clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market LB-001 from the FDA or other regulatory bodies, we cannot be certain that our product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing and distribution of genetic medicine products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations.

We are not permitted to market LB-001 in the United States until it receives approval of a BLA from the FDA, or in any foreign countries until it receives the requisite approval from such countries.

We have not submitted a BLA to the FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so for the foreseeable future.

LB-001 is our lead product candidate, and because any other product candidate would be based on similar technology, if LB-001 shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. Further, competitors may be developing products with similar technology and may experience problems with their products that could identify problems that would potentially harm our business.

We plan to file our IND to begin our first clinical trial for our MMA program targeting the liver in late-2019. Commencing this clinical trial, and any other clinical trials we may initiate, is also subject to finalizing the trial design based on discussions with the FDA and other regulatory authorities, including the NIH. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests, the start of our first clinical trial for our MMA programs or any of our other programs may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval

elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

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

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

Genomic medicines are novel, and any product candidates we develop may be complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products or otherwise harm our business.

Due to the novel nature of our platform, any product candidates we may develop will likely require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as the product candidates we intend to develop generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, European Union or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We or our third-party contractors also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to manage and/or provide the necessary oversight of our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations and prospects.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to meet market demand for any products we develop and commercialize.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could harm our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, EMA rules and regulations and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, additional integrity oversight and reporting obligations, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs, third-party manufacturers, suppliers and other contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters,

terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example, the loss of preclinical study or clinical trial data from completed, ongoing or planned 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 personal, confidential or proprietary information, we could incur liability and the further development of LB-001 or any other product candidate could be delayed.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

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

From time to time, we may publish interim "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Risks Related to Our Dependence on Third Parties

We currently contract with third parties for the manufacture and testing of materials. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We have manufacturing facilities to supply some of our discovery and preclinical research. We currently also rely on third-party manufacturers for the manufacture and some aspects of testing of our materials for preclinical studies and expect to continue to do so for clinical testing and for commercial supply of any product candidates that we may develop and for which we or our collaborators obtain marketing approval. We do not have a long term supply agreement with any of the third-party manufacturers, and we purchase our required supply on a purchase order basis. We are contracting with manufacturers that can produce the clinical and commercial supply of our product candidates.

We may be unable to establish any agreements with third-party manufacturers for clinical and commercial supply manufacturing, or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;

- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could harm our business, financial condition, results of operations and prospects.

Any medicines 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 regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are a few potential alternative manufacturers who could manufacture any product candidates we may develop, we may incur added costs and delays in identifying and qualifying any such replacement.

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

We intend to rely on third parties to conduct, supervise and monitor our clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner, it may harm our business.

We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. We intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we expect to have limited influence over their actual performance. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

We intend to rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. Our reliance on CROs for clinical development activities limits our control over these activities, but we will remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We and our CROs will be required to comply with the GLPs and GCPs, which are regulations and guidelines enforced by the FDA and are also required by the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and

clinical trial sites. If we or our CROs fail to comply with GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be sure 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 product produced under cGMP regulations. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process. We will also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other product development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If our relationship with any CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not harm on our business, financial condition, results of operations and prospects.

We may enter into collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates.

We may seek collaborative relationships for the development and commercialization of any product candidate we may develop. These collaborators could include large and mid-size pharmaceutical companies, regional and national 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 our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend partly on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Failure to obtain such collaborative relationships could impair the potential for any product candidate we may develop. We also will need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, such as:

- a collaboration partner may have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may delay clinical trials, provide insufficient funding for a clinical trial program, 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;
- a collaboration partner may seek to renegotiate or terminate its relationship with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our product candidates;
- a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate;
- a collaboration partner may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may terminate a strategic alliance and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources;
- a partner may use our products or technology in such a way as to invite litigation from a third party;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

If our collaborations do not result in the successful development and commercialization of products, or if one of our 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

product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described herein apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any product candidates we may develop. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement 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 several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us.

If conflicts arise between us and our collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our GeneRide technology. Additionally, because our current or future collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their

resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our GeneRide technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

If we fail to comply with obligations in agreements under which we in-license or acquire development or commercialization rights to products, technology or data from third parties, including our agreements with Stanford University and the University of Texas through which we license our core technology or our agreement with the NIH for development and commercial rights to the transgene for LB-001, we could lose such rights that are important to our business, and we may be unable to continue our development or commercialization programs as a result, which would be harmful to our business.

We are a party to agreements with Stanford University and the University of Texas to license our core technology, and we are party to a license agreement with the NIH for development and commercialization rights to the transgene for LB-001. We may enter into additional agreements with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

In exchange for the rights granted to us pursuant to the Stanford agreement, the University of Texas agreement and the NIH agreement, we are obligated to make payments upon the achievement of certain milestone events and to pay annual maintenance fees and specified royalties. If we fail to comply with our obligations under our agreements with Stanford University, the University of Texas, the NIH, or any future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for any product candidates and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our product candidates and our 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 platform technology and any proprietary product candidates and technology we develop. We seek to protect our proprietary position by in-licensing intellectual property relating to our platform technology and filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business. If we or our licensors are unable to obtain or maintain patent protection with respect to our AAV capsid technology and genome editing platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed. Additionally, if we do not adequately protect our intellectual property, our competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

No consistent policy regarding the scope of claims allowable in the field of gene therapy has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. Pending and future

patent applications may not result in issued patents which protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States.

The patent prosecution process is expensive, time-consuming, and complex. 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, or any future partners, collaborators or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities in time to obtain patent protection. Therefore, we may miss potential opportunities to strengthen our patent position. Additionally, although we enter into agreements containing non-disclosure and confidentiality obligations with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, collaborators, contract manufacturers, consultants, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If we or our partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain, or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees, or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance, or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions that will be claimed in our future patents or future patent applications, or that we will be the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions, or were the first to file for patent protection for them. If third parties have filed patent applications on inventions claimed in our patents or applications on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. 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.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or will file 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. Any patents that we hold or in-license may be challenged by third parties, narrowed, circumvented invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. 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. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting aBLAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable, or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. We have not had and do not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we license, and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

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. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. We or our licensors may in the future become subject to a third party pre-issuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or to other patent offices around the world. Alternately or additionally, we or our licensors may become involved in opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceedings and other similar proceedings in the United States or elsewhere, challenging our patent rights or the patent rights of others on which we rely to protect our business. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights; limit the duration of the patent protection of our technology and products; allow third parties to commercialize our technology or products and compete directly with us, without payment to us; or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us no license, develop or commercialize current or future product candidates. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, 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. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Pursuant to the terms of some of our license agreements with third parties, some of our third party licensors have the right, but not the obligation in certain circumstances to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors, and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection, or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

Moreover, some of our in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. Additionally some of our future patent filings may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could harm our competitive position, business, financial conditions, results of operations and prospects.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the U.S. government has certain rights, including march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention. For example, our licensors, including Stanford, have granted the U.S. government a non-exclusive, non-transferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States, the inventions described in certain of our in-licensed patents and patent applications, including certain aspects of our in-licensed nuclease-free genome editing technology. If the government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may permit the U.S. government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The U.S. government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our AAV capsid technology and GeneRide platform technology.

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 products in the future. 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. For example, pursuant to our license agreements with Stanford, the licensors may, under certain circumstances, grant a license to the patents that are the subject of such license agreements to a third party. Such third party would have full rights to the

patent rights that are the subject of such licenses, which could impact our competitive position and enable a third party to commercialize products similar to our future product candidates and technology. In addition, our rights to our in-licensed patents and patent applications may be dependent, in part, on inter-institutional or other operating agreements between the joint owners of such in-licensed patents and patent applications. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed patents and patent applications may be adversely affected, which could harm our competitive position, business, financial conditions, results of operations and prospects.

In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to our intellectual property licenses for certain patent families from Stanford, our licensors retain control of preparation, filing, prosecution, maintenance, and enforcement and defense of their patents and patent applications. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are subject of such licensed rights could be adversely affected.

Our licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could adversely affect our competitive position, business, financial conditions, results of operations, and prospects.

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

We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of product candidates and technologies we may develop.

In each of our license agreements, and we expect in our future agreements, we have the right under specified conditions to bring any actions against any third party for infringing on the patents we have exclusively licensed. Certain of our license agreements also require us to meet development thresholds and other obligations to maintain the license, including establishing a set timeline for developing and commercializing products. 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 on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and 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.

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. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

If we fail to comply with our obligations under our license agreements, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product or technology that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses. Any of these events could harm our competitive position, business, financial conditions, results of operations and prospects.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretations, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

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, including the amount, if any, that may become due and payable to our licensors in connection with any sublicense income. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If these events were to occur, they could harm our business, financial condition, results of operations and prospects.

We may not be successful in obtaining or maintaining necessary rights to current or future product candidates in clinical studies and for commercialization through acquisitions and in-licenses, which could delay or prevent us from commencing clinical trials and ultimately commercializing our current or future product candidates.

Because our programs may require the use of proprietary rights by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license, or use these proprietary rights.

Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of genome editing technology and filing patent applications potentially relevant to our business. In order to avoid infringing these third party patents, or patents that issue from these third party patent applications, we

may find it necessary or prudent to obtain licenses from such third party intellectual property holders. In addition, with respect to any patents we may co-own with third parties, we may require licenses to such co-owners' interest in such patents.

We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our technology and product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us or we may decide not to execute such option if we believe such license is not necessary to pursue our program. If we are unable or opt not to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

It is possible that we may be unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have at a reasonable cost or on reasonable terms. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or 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 candidate, which could harm our business, financial condition, results of operations, and prospects significantly.

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

Filing, prosecuting, and defending patents in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States or if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain 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 protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents, misappropriation of our other intellectual property rights, or marketing of competing products in violation of our intellectual property and proprietary rights generally.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts, resources and attention from other aspects of our business. Moreover, such proceedings 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. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and 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 or future owned patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process and after a patent has issued. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to some of our licensed intellectual property. In some 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 a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could harm our business, financial condition, results of operations and prospects.

Patent terms and data exclusivity for our product candidates may be inadequate to protect our competitive position for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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.

We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension) as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. The applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed. Additionally or alternatively, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical 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 is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States and other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents.

Recent patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs.

Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to challenge the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. The America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent

protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, the USPTO, and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could adversely affect our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. With respect to our GeneRide 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 our GeneRide 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 from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaborators, contract manufacturers, consultants, and other third parties. We also enter into agreements containing confidentiality and invention or patent assignment obligations with our employees and certain consultants. 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. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our business and competitive position could be materially and adversely harmed.

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

Competitors may infringe our intellectual property, such as our patents or trademarks, or the patents of our licensing partners. To counter infringement or unauthorized use, we may be required to file infringement claims. Additionally or alternatively, we may be required to defend against claims of infringement filed by third parties against us. In addition, our patents or the patents of our licensing partners may in the future become involved in inventorship, priority, or validity disputes. Filing infringement claims and countering and defending against claims regarding infringement or disputes of inventorship, priority, or validity can be expensive and time consuming and divert the time and attention of our management and scientific personnel.

If we or one of our licensors were to initiate legal proceedings against a third party, the defendant could counterclaim that such patent 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, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with

prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may in the future raise challenges to the validity of our patent 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, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings).

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 we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

In any patent infringement proceeding, there is a risk that a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, in whole or in part, or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in any litigation or proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly and may curtail or preclude our ability to assert those patents against third parties and exclude third parties from making and selling similar or competitive products. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy.

Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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 personnel from their normal responsibilities. The monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of shares 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. Moreover, there can be no assurance that we will have sufficient financial or other resources to conduct such litigation or proceedings adequately, which can last for years before they are concluded. 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 adversely affect our ability to compete in the marketplace.

The intellectual property landscape around genome editing technology is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could adversely affect the success of our business.

Our commercial success depends, in part, upon our ability and the ability of our collaborators to develop, manufacture, market, and sell our product candidates and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. However, the biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights, and our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Moreover, due to the intense research and development that is taking place by several companies, including us and our competitors, in the field of gene therapy, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property, and proprietary rights in the future. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, 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, which could be significant.

Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to products and methods of use for the treatment of the disease indications for which we are developing our product candidates. There may be third-party patents or patent applications with claims to materials, methods of manufacture, or methods for treatment related to the use or manufacture of our technologies and product candidates. If we are not able to obtain or maintain a license on commercially reasonable terms to any third-party patents that cover our product candidates or activities, such third parties could potentially assert infringement claims against us, which could harm our business.

Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on existing or future intellectual property rights. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. If any third-party patents or patent applications are found to cover our product candidates or their methods of use, we may not be free to manufacture or market our product candidates as planned without obtaining a license.

Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. 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 product candidates we may develop and any other product candidates or technologies covered by the asserted third party patents.

The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the asserted patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence as to the invalidity of any such U.S. patent claim to overcome the presumption of validity enjoyed by issued patents. There is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we may develop and our 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. Alternatively or additionally, it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. We also 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 commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar adverse effect on our business, financial condition, results of operations, and prospects.

We may be subject to claims that we, 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 and our licensors' employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, some of which may be our competitors or potential competitors. Some of these individuals executed agreements containing proprietary rights, non-disclosure and non-competition obligations, or similar agreements, in connection with such current or previous employment. 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 we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and consultants 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 we fail in prosecuting or defending any such claims listed above, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 gene therapy products that are similar to any product candidates we may develop or utilize similar gene therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- others may be able to make or utilize gene therapy technology that functions as a viable alternative to technology we may develop or technology covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future 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 our license partners or current or future 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 harm our business; and
- we may choose not to file a patent in order to maintain 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 harm our business, financial condition, results of operations, and prospects.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Healthcare legislative reform measures and constraints on the national budget for social security systems may harm our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell any products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or the Affordable Care Act, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees for certain branded prescription drugs and provided incentives to programs that increase the federal government's comparative effectiveness research.

Some of the provisions of the Affordable Care Act have yet to be implemented, while certain provisions have been subject to legal and political challenges. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the Affordable Care Act. In December 2017, Congress repealed the tax penalty for an individual's failure to maintain Affordable Care Act-mandated health insurance as part of a tax reform bill. Further, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-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. Moreover, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress could consider additional legislation to repeal or replace elements of the Affordable Care Act, or adopt other healthcare reform measures. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation. Thus, the full impact of the Affordable Care Act, any law replacing elements of it, and the political uncertainty surrounding any repeal or replacement legislation on our business remains unclear.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our drug product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any denial in coverage or reduction in reimbursement from Medicare or other government programs may result in a similar denial or reduction in payments from private payors, which may adversely affect our future profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties and other sanctions.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or 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, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare professionals and entities and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, additional integrity reporting and oversight obligations, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations, any of which could harm our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

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 prohibited in the European Union.

Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publically disclosed. 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare 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 healthcare 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 administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could harm our business, financial condition, results of operations, and prospects.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws, regulations, and permitting requirements. These current or future laws, regulations, and permitting requirements may impair our research, development, or production efforts. Failure to comply with these laws, regulations, and permitting requirements also may result in substantial fines, penalties, or other sanctions or business disruption, which could harm our reputation, business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could harm our reputation, business, financial condition, results of operations and prospects.

Risks Related to Employee Matters and Managing Growth

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Fred Chereau, our President and Chief Executive Officer, and Dean Falb, our Chief Scientific Officer, as well as the other members of our management, technical, scientific, clinical and regulatory teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific, technical and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific, technical, clinical and regulatory advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2018, we had 23 employees. We expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, technical development, clinical and regulatory affairs and sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

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.

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

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

Risks Related to Commercialization

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new genetic medicine products is highly competitive. Moreover, the gene editing field is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our focus is the development of genetic medicines. There are a number of companies developing nuclease-based gene editing technologies, including CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Sangamo Therapeutics and Precision BioSciences. We may also compete with companies developing gene therapy products, including Homology Medicines, Audentes Therapeutics, bluebird bio, uniQure and Voyager Therapeutics. Any products we may develop could also face competition from other products approved to treat the same disease based on other types of therapies, such as small molecule, antibody or protein therapies. There are several companies developing competing products that target MMA, the indication for which we are developing LB-001. These companies include Moderna Therapeutics with an mRNA based approach, Selecta Biosciences with AAV gene therapy, and Hemoshear Therapeutics using a small molecule. While none of these companies have clinical-stage programs for these therapies, any of them may obtain regulatory approval for a treatment for MMA before LB-001, which could negatively affect our ability to successfully commercialize LB-001, if approved.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our 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 or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly 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 potential product candidates uneconomic or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by third-party payors, including governmental healthcare programs such as Medicare and Medicaid, managed care organizations and private health insurers are essential for most patients to be able to afford prescription medications such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by third-party payors will have an effect on our ability to successfully commercialize our product candidates. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. In the United States, third-party payors, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how third-party payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor and coverage and reimbursement by one payor does not guarantee coverage and reimbursement by another payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe

and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional 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 product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits. Furthermore, some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Due to the novel nature of our technology and the potential for any product candidates we may develop to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.

Our initial target patient populations are relatively small, and, as a result, the pricing and reimbursement of any product candidates we may develop, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any product candidates we may develop (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products. In addition, it may be necessary for us to develop new reimbursement models in order to realize adequate value. Third-party payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations and prospects could be adversely affected.

We expect the cost of a single administration of genomic medicine products, such as those we are seeking to develop, to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by third-party payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of any product candidates we may develop will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

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

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data.

We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates we may develop. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

If the market opportunities for any product candidates we may develop are smaller than we believe they are, our revenues, if any, may be adversely affected, and our business may suffer. Because the target patient populations for many of the product candidates we may develop are small, we must be able to successfully identify patients and achieve a significant market share to achieve and maintain profitability and growth.

We focus our research and product development on treatments for rare pediatric diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our products, or may become increasingly difficult to identify or gain access to, all of which could harm our business, financial condition, results of operations, and prospects.

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

If LB-001 or any other product candidate we may develop is approved for commercialization, it may be marketed in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization in foreign countries;
- reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- foreign reimbursement, pricing and insurance regimes;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including floods and fires.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the European Union and many of the individual countries in Europe with which we will need to comply. Many U.S.-based biotechnology companies have found the process of marketing their own products in Europe to be very challenging.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Affordable Care Act 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-licensed 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 licensed 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 licensed. 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 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 their 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. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could adversely affect the future commercial prospects for our biological products.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or 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.

Risks Related to Our Common Stock

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

Our stock price may be volatile. The stock market in general, and the market for pharmaceutical and biopharmaceutical companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of companies whose stock is experiencing those price and volume limitations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual performance. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price at which they purchased them. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- timing and results of clinical trials of any product candidate we may develop or those of our competitors;
- developments related to our collaborations;
- regulatory actions with respect to any product candidate we may develop or our competitors' products and product candidates;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- failure or discontinuation of any of our product development and research programs;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- 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;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- results of preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;

- variations in our financial results, development timelines, or recommendations by securities analysts, or those of companies that are perceived to be similar to us;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- limited public float;
- expiration of market stand-off or lock-up agreement;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- developments or changing views regarding the use of genomic medicines, including those that involve genome editing;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section and others beyond our control.

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

As of December 31, 2018, our executive officers and directors, combined with our stockholders who owned more than 5% of our common stock, together with their respective affiliates, beneficially owned approximately 44% of our outstanding common stock, including shares subject to outstanding options that are exercisable within 60 days after such date. Accordingly, these stockholders are able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of entrenching our management or board of directors, delaying or preventing a change in control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

A significant portion of our total outstanding shares are eligible to 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 doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2018, 15,020,933 shares of our common stock were restricted as a result of securities laws or lock-up agreements, but will become eligible to be sold at various times beginning 180 days after the date of our initial public offering, or IPO, unless held by one of our affiliates, in which case the resale of those securities will be subject to volume limitations under Rule 144 of the Securities Act of 1933, as amended, or Rule 144. Moreover, holders of an aggregate of 11,789,775 shares of our common stock have rights, subject to specified 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, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We also plan to register all shares of common stock that we may issue under our equity compensation plans or that are issuable upon the exercise of outstanding options. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of our IPO. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and golden parachute payments.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected to "opt out" of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance, or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

We are incurring significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a newly public company, we are incurring significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices.

We expect that we will need to hire additional accounting, finance and other personnel in connection with our efforts of continuing to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and make some activities more time-consuming and costly.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, 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 SOX 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, potentially engage outside consultants, 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 whether such 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 we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to successfully remediate these material weaknesses in our internal control over financial reporting, it could have an adverse effect on our company.

We have identified certain material weaknesses in our internal control over financial reporting. These material weaknesses include: (1) an ineffective control environment, including a lack of sufficient accounting personnel and personnel with financial reporting expertise; (2) ineffective controls procedures, including those related to recognition in the appropriate period for certain transactions; (3) ineffective risk assessment controls, including those policies and practices that would identify changes in our business practices, which could significantly impact our consolidated financial statements and system of internal controls; and (4) ineffective monitoring of controls related to the financial close and reporting process. Had we performed an evaluation of our internal control over financial reporting in accordance with Section 404, additional control deficiencies may have been identified by management, and those control deficiencies could have also represented one or more material weaknesses.

In an effort to remediate these material weaknesses, we have begun hiring additional accounting and finance personnel. We have also retained an accounting consulting firm to provide additional depth and breadth in our technical accounting and financial reporting capabilities. We intend to continue this arrangement until additional permanent technical accounting resources are identified and hired. We intend to formalize our policies and procedures surrounding our financial close, financial reporting and other accounting processes. We intend to further develop and document necessary policies and procedures regarding our internal control over financial reporting, such that we are able to perform a Section 404 analysis of our internal control over financial reporting when and as required. We are in the process of recruiting additional qualified accounting and finance personnel to provide needed levels of expertise in our internal accounting function. We cannot be sure that these measures will significantly improve or remediate the material weaknesses described above. We also cannot be sure that we have identified all or that we will not have additional material weaknesses in the future. Accordingly, material weaknesses may still exist when we report on the effectiveness of our internal control over financial reporting for purposes of our attestation when required by reporting requirements under the Exchange Act or Section 404. Further, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

We expect to incur additional costs to remediate these control deficiencies, though there can be no assurance that our efforts will be successful or avoid potential future material weaknesses. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, 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 stock price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC or other regulatory authorities.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have, and may never obtain, research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our restated certificate of incorporation and restated by-laws and under Delaware law could make an acquisition of our company, 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 restated certificate of incorporation and our restated by-laws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also 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, our restated certificate of incorporation and our restated by-laws include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, 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.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that our stockholders could receive a premium for their common stock in an acquisition.

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

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock would be the sole source of gain on an investment in our common stock for the foreseeable future.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

Recently-enacted U.S. tax legislation has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, and revising the rules governing net operating losses. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service, any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses U.S. federal taxable income as a starting point for computing state and local tax liabilities.

The reduction of the corporate tax rate under the legislation may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Furthermore, under the legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond will only be able to offset 80% of taxable income. This change may require us to pay U.S. federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

While some of the changes made by the tax legislation may adversely affect the Company in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be

re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal controls and procedures for compliance with SOX Section 404, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our common share price and make it more difficult for us to effectively market and sell our service to new and existing customers.

Our certificate of incorporation and bylaws designate the state or federal courts in the State of Delaware and the federal district courts of the United States, respectively, as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that, unless our board of directors otherwise determines, the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to our company or our stockholders, any action asserting a claim against us or any of our directors or officers arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or by-laws, or any action asserting a claim against us or any of our directors or officers governed by the internal affairs doctrine. Additionally, our bylaws provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against us and our directors and officers. However, as previously disclosed in our Current Report on Form 8-K filed with the SEC on February 28, 2018, in light of the decision issued by the Delaware Court of Chancery in *Sciabacucchi v. Salzberg*, C.A. No. 2017-0931-JTL (Del. Ch.), finding that provisions such as the federal forum selection provision in our bylaws are not valid under Delaware law, we do not intend to enforce such provision unless and until the Delaware Court of Chancery's decision is reversed by the Delaware Supreme Court on appeal or otherwise abrogated. We may incur additional costs associated with resolving such actions in other jurisdictions, which could adversely affect our results of operations and financial condition.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We occupy approximately 11,800 square feet of office and laboratory space in Cambridge, MA under a short term lease. While we expect that this space will be sufficient to cover our needs until the lease expires, we are actively looking for a longer term lease for laboratory space.

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades on The Nasdaq Global Market under the symbol "LOGC." As of March 29, 2019, there were approximately 24 holders of record of shares of our common stock

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future.

Use of Proceeds

On October 23, 2018, we closed our IPO, in which we issued and sold 8,050,000 shares of our common stock, including 1,050,000 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $10.00 per share for gross proceeds of $80.5 million, before deducting underwriting discounts and commissions and offering expenses payable by us. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-227523), which was declared effective by the SEC on October 18, 2018. Jefferies LLC, Barclays Capital Inc. and William Blair & Company, L.L.C. acted as joint book-running managers of the offering and as representatives of the underwriters. Chardan Capital Markets, LLC acted as the lead manager for the offering. The offering commenced on October 18, 2018 and did not terminate until the sale of all of the shares offered.

The net offering proceeds to us, after deducting underwriting discounts and offering costs payable by us of an aggregate of approximately $8.2 million, were approximately $72.3 million. No material offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on October 18, 2018. As of December 31, 2018, we consumed approximately $5.0 million of net proceeds from the IPO, primarily to continue ongoing development of LB-001 in MMA and for discovery and preclinical development of additional product candidates, and for working capital and general corporate purposes. We invested the remaining funds received in cash equivalents.

Item 6. Selected Financial Data

The following tables set forth our selected financial data for the periods indicated. The following consolidated statement of operations data for the years ended December 31, 2018 and 2017 and the consolidated balance sheet data as of December 31, 2018 and 2017 are derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the year ended December 31, 2016 and the consolidated balance sheet data as of December 31, 2016 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of results to be expected for any period in the future. The data should be read together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in conjunction with the consolidated financial statements, related notes and other financial information included elsewhere in this Annual Report on Form 10-K. The selected financial data in this section are not intended to replace our financial statements and the related notes thereto.

Consolidated Statement of Operations Data:

	Year Ended December 31,		
(in thousands, except shares and per share data)	2018	2017	2016
Operating expenses:			
Research and development	$ 11,079	$ 3,558	$ 2,030
General and administrative	6,864	2,296	1,373
Total operating expenses	17,943	5,854	3,403
Loss from operations	(17,943)	(5,854)	(3,403)
Other income (expense):			
Interest income (expense), net	567	54	(1)
Other (expense) income, net	(159)	67	(6)
Total other income (expense), net	408	121	(7)
Loss before income taxes	(17,535)	(5,733)	(3,410)
Income tax provision	(86)	(62)	(18)
Net loss	$ (17,621)	$ (5,795)	$ (3,428)
Net loss attributable to common stockholders—basic and diluted	$ (17,621)	$ (7,735)	$ (3,765)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.04)	$ (5.54)	$ (4.43)
Weighted-average common stock outstanding—basic and diluted	5,801,533	1,395,381	849,061

Consolidated Balance Sheet Data:

	As of December 31,		
	2018	2017	2016
		(in thousands)	
Cash and cash equivalents	$80,906	$24,575	$ 1,728
Total assets	$82,910	$26,174	$ 2,029
Total liabilities	$ 2,685	$ 1,711	$ 920
Total stockholders' equity (deficit)	$80,225	$ (8,599)	$(3,250)

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, these forward-looking statements.

Overview

We are a genome editing company focused on developing medicines to durably treat rare diseases in patients with significant unmet medical need using GeneRide, our proprietary technology platform. Our GeneRide technology is designed to precisely integrate corrective genes into a patient's genome to provide a stable therapeutic effect. Because GeneRide is designed to have this durable therapeutic effect, we are initially targeting rare liver disorders in pediatric patients where it is critical to provide treatment early in a patient's life before irreversible disease pathology can occur. We have demonstrated proof of concept of our therapeutic platform in animal models for a number of diseases and are focusing on development of our lead product candidate, LB-001, for the treatment of Methylmalonic Acidemia, or MMA, a life-threatening disease that presents at birth.

Based on our GeneRide technology, we are developing our lead product candidate, LB-001, to treat MMA. We plan to advance LB-001 to an IND filing by the end of 2019 and into a Phase 1/2 clinical trial in pediatric MMA patients in 2020. We believe that achieving clinical proof of concept in an inherited liver disease such as MMA will validate our platform technology, including its potential application to other organs and diseases. In addition to MMA, we have demonstrated proof of concept of our platform in hemophilia B, alpha-1-antitrypsin deficiency, or A1ATD, and Crigler-Najjar syndrome animal disease models. We expect to select future product candidates from these genetic diseases or others addressed by targeting the liver initially, and later by targeting the CNS and muscle.

Since our inception in 2014, we have devoted all of our efforts to business planning, research and development, developing and protecting our intellectual property, raising capital, recruiting management and technical staff. We do not have any products approved for sale and have not generated any revenue. As of December 31, 2018, we have raised approximately $72.3 million in net proceeds through our initial public offering, or IPO, in October 2018 and approximately $33.1 million in net proceeds from the sale of our convertible preferred stock in 2016 and 2017. We have incurred significant operating losses since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and commercialization of one or more of our product candidates. Our net losses were $17.6 million and $5.8 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $27.2 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future in connection with our ongoing activities.

Furthermore, we now incur additional costs associated with operating as a public company that we did not previously incur or had previously incurred at lower rates as a private company, including significant legal, accounting, investor relations and other expenses.

Initial Public Offering

On October 23, 2018, we completed our IPO, in which we issued and sold 8,050,000 shares of common stock, including 1,050,000 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $10.00 per share. The aggregate net proceeds to us from the IPO

were approximately $72.3 million after deducting underwriting discounts and commissions and offering expenses. The shares began trading on The Nasdaq Global Market on October 19, 2018. Upon completion of the IPO, all of our outstanding shares of convertible preferred stock, converted into 11,789,775 shares of our common stock.

Components of Results of Operations

Revenue

Since inception through December 31, 2018, we have not generated any revenue. We do not expect to generate any revenue from the sale of products in the near future. If our development efforts for LB-001, or other product candidates that we may develop in the future, are successful and result in regulatory approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our product candidates, and include:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- license maintenance fees and milestone fees incurred in connection with various license agreements;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and, eventually, clinical trial materials;
- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, as well as academic institutions and consultants that conduct our preclinical studies and other scientific development services;
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses; and
- costs related to compliance with regulatory requirements.

We expense research and development costs as incurred. Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase for the foreseeable future as we initiate clinical trials for our product candidate LB-001 and continue to discover and develop additional product candidates. If any of our product candidates enter into later stages of clinical development, they will generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and

administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, travel expenses, and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax compliance services, director and officer insurance costs; and investor and public relations costs.

Other Income (Expense), Net

Interest income (expense), net consists primarily of interest on our cash and cash equivalents. Other (expense) income, net consists primarily of foreign exchange gains and losses.

Results of Operations

Year Ended December 31, 2018 and 2017

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

	Year Ended December 31,	
	2018	2017
	(in thousands)	
Operating expenses:		
Research and development	$ 11,079	$ 3,558
General and administrative	6,864	2,296
Total operating expenses	17,943	5,854
Loss from operations	(17,943)	(5,854)
Other income:		
Other income, net	408	121
Loss before income taxes	(17,535)	(5,733)
Income tax provision	(86)	(62)
Net loss	$(17,621)	$(5,795)

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	Increase
		(in thousands)	
LB-001 external development and manufacturing costs	$ 3,628	$ 179	3,449
Personnel-related costs	2,366	1,392	974
Other research and development costs	5,085	1,987	3,098
Total research and development expenses	$11,079	$3,558	$ 7,521

Research and development expenses for the year ended December 31, 2018 were $11.1 million, compared to $3.6 million for year ended December 31, 2017. The increase of approximately $7.5 million was primarily due to an increase of approximately $3.4 million related to external development and manufacturing expenses for our lead product candidate LB-001, $3.1 million in other research and development expenses as we increased our overall research and development activities, and $1.0 million in personnel-related costs related to an increase in headcount. Personnel-related costs for the year ended December 31, 2018 included stock-based compensation expense of $0.3 million compared to $0.4 million for the year ended December 31, 2017.

General and Administrative Expenses

General and administrative expenses were $6.9 million for the year ended December 31, 2018, compared to $2.3 million for the year ended December 31, 2017. The increase of approximately $4.6 million was primarily due to legal and professional fees and personnel-related costs, including salaries, stock-based compensation and bonuses. The increase in professional fees was primarily due to the increase in legal, auditing and consulting services provided. The increase in personnel-related costs was primarily due to an increase in headcount of executive level employees. Stock-based compensation expense included in general and administrative expenses was $0.8 million and $0.1 million for the years ended December 31, 2018 and 2017, respectively.

Other Income, Net

Other income, net was $0.4 million for the year ended December 31, 2018, compared to other income, net of $0.1 million for the year ended December 31, 2017. The change was primarily related to interest earned on our money market accounts.

Liquidity and Capital Resources

Overview

Since our inception and through December 31, 2018, we have not generated any revenue and have incurred significant losses and negative cash flows from our operations.

Cash Flows

The following table summarized our cash flows for each of the years ended December 31, 2018 and 2017:

	Year Ended December 31,	
	2018	2017
	(in thousands)	
Net cash used in operating activities	$(15,267)	$ (5,782)
Net cash used in investing activities	(579)	(36)
Net cash provided by financing activities	72,306	28,703
Effect on foreign exchange rates on cash and cash equivalents	17	(38)
Net increase in cash and cash equivalents	$ 56,477	$22,847

Operating Activities

During the year ended December 31, 2018, operating activities used $15.3 million of cash, primarily from our net loss of $17.6 million and net cash provided by changes in our operating assets and liabilities of $1.0 million, non-cash charges of $1.3 million, which were primarily related to stock-based compensation expense and loss on disposal of property and equipment. Changes in net cash in our operating assets and liabilities for the year ended

December 31, 2018 consisted primarily of a $0.2 million increase to prepaid expenses and other current assets, a $0.9 million increase in accrued expenses and other liabilities and a $0.2 million decrease to other non-current assets. The increase in accrued expenses was primarily due to the increase in accrued professional services mainly related to the IPO.

During the year ended December 31, 2017, operating activities used $5.8 million of cash, primarily from our net loss of $5.8 million and net cash used by changes in our operating assets and liabilities of $0.5 million, partially offset by non-cash charges of $0.5 million, primarily related to stock-based compensation expense. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2017 consisted primarily of a $1.0 million increase in prepaid expenses and other current assets and a $0.2 million increase in other non-current assets, which were partially offset by an increase of $0.8 million in accounts payable. The increases in prepaid expenses and other current assets and other non-current assets were primarily due to an increase in prepayments related to our research agreements. The increase in accounts payable was primarily due to an increase in spending related to LB-001.

Investing Activities

During the year ended December 31, 2018, net cash used in investing activities was $0.6 million, primarily from the purchase of property and equipment.

During the year ended December 31, 2017, net cash used in investing activities was $36,000 for the purchase of property and equipment.

Financing Activities

During the year ended December 31, 2018, net cash provided by financing activities was $72.3 million, primarily from the issuance of common stock related to the IPO.

During the year ended December 31, 2017, net cash provided by financing activities was $28.7 million, primarily from net proceeds from the sale of the first tranche of Series B preferred stock in June 2017.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. We expect that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of any product candidates from our current research programs;
- initiate clinical trials for LB-001 and any other product candidates we identify and develop;
- seek to identify, assess, acquire and/or develop additional research programs and additional product candidates;
- seek marketing approvals for any product candidate that successfully complete clinical trials;
- develop, optimize, scale and validate a manufacturing process and analytical methods for any product candidates we may develop;
- establish and build out internal process and analytical development capabilities and research and preclinical grade production;
- obtain market acceptance of any product candidates we may develop as viable treatment options;
- address competing technological and market developments;

- maintain, expand and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- further develop our GeneRide technology platform;
- hire additional technical, quality, regulatory, clinical, scientific and commercial personnel; add operational, financial and management information systems and personnel, including personnel to support our process and product development, manufacturing and planned future commercialization efforts;
- make royalty, milestone or other payments under current and any future in-license agreements;
- establish and maintain supply chain and manufacturing relationships with third parties that can provide adequate products and services, in both amount, timing and quality, to support clinical development and the market demand for any product candidate for which we obtain regulatory and marketing approval;
- leasing and building new facilities, including offices and labs, to support organizational growth;
- validate and build-out a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval.

Because of the numerous risks and uncertainties associated with the development of LB-001 and other product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the initiation, scope, progress, timing, costs and results of drug discovery, preclinical development, laboratory testing, and planned clinical trials for LB-001 and any other product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the U.S. Food and Drug Administration, or FDA, and other comparable foreign regulatory authorities, including resolving any potential clinical holds that may be imposed on us;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions;
- the achievement of milestones or occurrence of other developments that trigger payments under any of our current agreements or other agreements we may enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical or commercial-scale manufacturing activities;
- the extent to which we in-license or acquire other products and technologies;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the cost of establishing sales, marketing and distribution capabilities for LB-001 and any other product candidates in regions where we choose to commercialize our product candidates, if approved; and

- the initiation, progress, timing and results of our commercialization of LB-001 and any other product candidates, if approved, for commercial sale.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant trial delays due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development. We may never succeed in obtaining regulatory approval for any of our product candidates.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through offerings of securities, private equity financing, debt financings, collaborations, government contracts or other strategic transactions. The terms of financing may adversely affect the holdings or the rights of our stockholders. If we are unable to obtain funding, we may be required to delay, limit, reduce or terminate some or all of our research and product development, product portfolio expansion or future commercialization efforts.

We will also continue to incur costs as a public company that we did not previously incur or have previously incurred at lower rates, including increased fees payable to the non-employee members of our board of directors, increased personnel costs, increased director and officer insurance premiums, audit and legal fees, investor relations fees and expenses for compliance with public company reporting requirements under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and rules implemented by the SEC and Nasdaq.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2018:

	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	$1,251	$ 1,028	$223	$ —	$ —
Collaboration and research agreements (1)	1,268	1,268	—	—	—
Total	$2,519	$ 2,296	$223	$ —	$ —

(1) Represents license and research fees under our collaboration and research agreements. These amounts do not include any potential contingent payments, including those due upon the achievement by us of specified clinical, regulatory and commercial events, as applicable, or patent prosecution, royalty payments or license and research fees we may be required to make under license agreements we have entered into with various entities, including Stanford, the University of Texas and other research institutions. We have excluded these potential payments in the contractual obligations table because the timing and likelihood of these contingent payments are not currently known and would be difficult to predict or estimate.

We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials and preclinical research studies and testing. Manufacturing commitments in the preceding table include agreements that are enforceable and legally binding on us and that specify all significant terms, including fixed or minimum quantities to be purchased; fixed, minimum or variable price provisions; and the approximate timing of the transaction. For obligations with cancellation provisions, the amounts included in the preceding table are limited to the non-cancelable portion of the agreement terms or the minimum cancellation fee.

We may incur potential contingent payments upon our achievement of clinical, regulatory and commercial milestones, as applicable, or royalty payments that we may be required to make under license agreements we

have entered into with various entities pursuant to which we have in-licensed certain intellectual property. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid by us are not fixed or determinable at this time and are excluded from the table above.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been 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 assumptions that affect the reported amounts of assets and liabilities, costs 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 greater 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. 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. 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. 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.

Stock-Based Compensation

We account for stock-based compensation transactions using a grant-date fair-value-based method under FASB Codification Topic 718, Compensation—Stock Compensation. We account for all stock-based awards granted to employees and non-employees based on their fair value on the date of the grant and recognize compensation expense of those awards, over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions. We have also issued restricted stock with performance-based vesting conditions and recorded the expense for these awards when we concluded that it was probable that the performance condition would be achieved. Stock-based compensation is classified in the accompanying statements of operations based on the function to which the related services are provided. We recognize stock-based compensation expense for the portion of awards that have vested. Forfeitures are accounted for as they occur.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

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 have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Recently Issued Accounting Pronouncements

Refer to Note 2 in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a discussion of recent accounting pronouncements.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities and foreign currency exchange rate sensitivities.

Interest Rate Sensitivity

As of December 31, 2018, we had cash and cash equivalents of $80.9 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.S. bank interest rates. Our surplus cash has been invested in interest-bearing savings accounts from time to time. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

As of December 31, 2018, we had no debt outstanding and are therefore not subject to interest rate risk related to debt.

Foreign Currency Exchange Risk

The functional currency of our wholly owned foreign subsidiary, LogicBio Research, is in the Israeli new shekel. Assets and liabilities of LogicBio Research are translated into United States dollars at the exchange rate in effect on the consolidated balance sheet date. Income items and expenses are translated at the average exchange rate in effect during the period. Stockholders' equity (deficit) amounts are translated based on historical exchange rates as of the date of each transaction. Unrealized translation gains and losses are recorded as a foreign currency translation adjustment and included in the consolidated statements of convertible preferred stock and stockholder's deficit as a component of accumulated other comprehensive loss. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in other (expense) income, net in the consolidated statements of operations as incurred. As of December 31, 2018, all operations had ceased for LogicBio Research.

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Item 8. Financial Statements and Supplementary Data.

Our financial statements, together with the report of our independent registered public accounting firm, appear in this Annual Report on Form 10-K beginning on page F-1.

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of December 31, 2018. Our disclosure controls and procedures are designed to ensure that information we are required to disclose in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures, and is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms.

Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures as of December 31, 2018 were not effective due to the material weakness identified in fiscal year 2017 in our internal control over financial reporting process which included an ineffective control environment, including a lack of sufficient accounting personnel and personnel with financial reporting expertise, ineffective controls procedures, including those related to recognition in the appropriate period for certain transactions, ineffective risk assessment controls, including those policies and practices that would identify changes in our business practices, which could significantly impact our consolidated financial statements and system of internal controls, and ineffective monitoring of controls related to the financial close and reporting process.

Remediation Plan

We are committed and are taking steps necessary to remediate the control deficiencies that constituted the above material weakness by implementing changes to our internal control over financial reporting. During 2018, we made the following enhancements to our control environment including the following:

- We added finance personnel to the organization to strengthen our internal accounting team to include a Controller.
- We engaged a third party to help us enhance our documentation of accounting policies and positions on technical accounting topics throughout the year.

Our remediation activities are continuing during 2019. In addition to the above actions, we expect to engage in additional activities in the current year, including:

- Add more accounting resources to enhance our control environment;
- Engage outside consultants to assist in the design, implementation, and documentation of internal controls that address the relevant risks, are properly designed, and provide for appropriate evidence of performance of the internal control;
- Engage outside consultants to assist us in the evaluation of our information systems to determine if there are internal control gaps that should be addressed in the general information technology controls and implement any needed improvements for existing systems;

- Continue to engage external consultants to provide support related to more complex applications of GAAP and document and assess our accounting policies and procedures;
- Enhance the execution of our risk assessment activities by evaluating whether the design of our internal controls appropriately address changes in the business and that could impact our system of internal controls; and,
- Engage outside consultants to perform tests of our system of internal controls to monitor the operating effectiveness of operation of our internal controls and to gain assurance whether such controls are present and functioning.

We continue to redesign and implement internal control activities. We continue to establish policies and procedures and enhance corporate oversight over process-level controls and structures to ensure that there is appropriate assignment of authority, responsibility, and accountability to enable remediating our material weaknesses.

We believe that our remediation plan will be sufficient to remediate the identified material weakness and strengthen our internal control over financial reporting. As we continue to evaluate, and work to improve, our internal control over financial reporting, management may determine that additional measures to address control deficiencies or modifications to the remediation plan are necessary. We cannot assure you, however, when we will remediate such weaknesses, nor can it be certain whether additional actions will be required or the costs of any such actions. Moreover, we cannot assure you that additional material weaknesses will not arise in the future.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act.

Changes in Internal Control over Financial Reporting

Except for the remediation efforts of the previously identified material weakness as described above, there were no changes in our internal control over financial reporting that occurred during the fourth quarter of the year ended December 31, 2018 that materially affected, or were 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 "Section16(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 and is incorporated herein by reference.

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 under the captions "Employment Agreements," "Potential Payments Upon Termination or Change in Control," "Board Determination of Independence" and "Related Person Transactions" 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 Accountant 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 Statements and Schedules.

(a)(1) Financial Statements.

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements in this Annual Report on Form 10-K, which is incorporated into this Item 15 by reference.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto.

(a)(3) Exhibits.

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished.

Number	Description
3.1	Fourth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No.001-38707, filed on October 29, 2018).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, File No.001-38707, filed on October 29, 2018).
4.1	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
4.2	Investors' Rights Agreement, dated as of June 19, 2017, by and among LogicBio Therapeutics, Inc. and each of the Investors and Common Holders listed therein (incorporated by reference to Exhibit 4.2 to the Company's S-1, File No. 333-227523, filed on September 25, 2018).
10.1#	Amended and Restated Exclusive (Equity) Agreement dated January 31, 2018, between The Board of Trustees of the Leland Stanford Junior University and LogicBio Therapeutics, Inc. (incorporated by reference to Exhibit 10.1 to the Company's S-1, File No. 333-227523, filed on September 25, 2018).
10.2#	Patent & Technology License Agreement, dated May 7, 2018, by and between LogicBio Therapeutics, Inc. and The Board of Regents of the University of Texas System (incorporated by reference to Exhibit 10.2 to the Company's S-1, File No. 333-227523, filed on September 25, 2018).
10.3+*	Patent License Agreement dated December 14, 2018, between the U.S. Department of Health and Human Services, as represented by the National Human Genome Research Institute, an Institute of the National Institutes of Health and LogicBio Therapeutics, Inc.
10.4†	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.3 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.5†	LogicBio Therapeutics, Inc. 2014 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.4 to the Company's S-1, File No. 333-227523, filed on September 25, 2018).
10.6†	Form of Stock Option Agreement under the LogicBio Therapeutics, Inc. 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.7†	Form of Restricted Stock Agreement under the LogicBio Therapeutics, Inc. 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).

Number	Description
10.8	Consulting Agreement with Mark Kay, dated April 1, 2018 (incorporated by reference to Exhibit 10.8 to the Company's S-1, File No. 333-227523, filed on September 25, 2018).
10.9†	LogicBio Therapeutics, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.8 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.10†	LogicBio Therapeutics, Inc. 2018 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.9 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.11†	LogicBio Therapeutics, Inc. 2018 Cash Incentive Plan (incorporated by reference to Exhibit 10.10 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.12†	Form of Incentive Stock Option Agreement under the LogicBio Therapeutics, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.13†	Form of Non-Statutory Stock Option Agreement under the LogicBio Therapeutics, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.14†	Form of Amended and Restated Executive Employment Agreement, by and between LogicBio Therapeutics, Inc. and Frederic Chereau (incorporated by reference to Exhibit 10.13 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.15†	Form of Amended and Restated Executive Employment Agreement, by and between LogicBio Therapeutics, Inc. and Matthias Jaffé (incorporated by reference to Exhibit 10.14 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
10.16†	Form of Amended and Restated Executive Employment Agreement, by and between LogicBio Therapeutics, Inc. and Tom Wilton (incorporated by reference to Exhibit 10.15 to the Company's S-1/A, File No. 333-227523, filed on October 9, 2018).
21.1*	Subsidiaries of LogicBio Therapeutics, Inc.
31.1*	Rule 13a—14(a) / 15d—14(a) Certifications—Chief Executive Officer.
31.2*	Rule 13a—14(a) / 15d—14(a) Certifications—Chief Financial Officer.
32.1**	Section 1350 Certifications.
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.

* Filed herewith.
** Furnished herewith.
† Indicates a management contract or compensatory plan.
+ Application has been made to the Securities and Exchange Commission for confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.
# Portions of the exhibit (indicated by asterisks) have been omitted pursuant to a confidential treatment order granted by the Securities and Exchange Commission.

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

LOGICBIO THERAPEUTICS, INC.

Date: April 1, 2019

By: /s/ Frederic Chereau
Frederic Chereau
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Frederic Chereau Frederic Chereau	President, Chief Executive Officer and Director *(Principal Executive Officer)*	April 1, 2019
/s/ Matthias Jaffé Matthias Jaffé	Chief Financial Officer *(Principal Financial and Accounting Officer)*	April 1, 2019
/s/ Leon Chen Leon Chen, Ph.D.	Director	April 1, 2019
/s/ Erez Chimovits Erez Chimovits	Director	April 1, 2019
/s/ Sofia Ioannidou Sofia Ioannidou Ph.D.	Director	April 1, 2019
/s/ Tomer Kariv Tomer Kariv	Director	April 1, 2019
/s/ Mark Kay Mark Kay, M.D., Ph.D.	Director	April 1, 2019
/s/ Richard Moscicki Richard Moscicki, M.D.	Director	April 1, 2019
/s/ Daniel O'Connell Daniel O'Connell, M.D., Ph.D.	Director	April 1, 2019
/s/ Michael Wyzga Michael Wyzga	Director	April 1, 2019

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of LogicBio Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of LogicBio Therapeutics, Inc. and subsidiaries (the "Company") as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the 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 each of the two years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

Our audits included performing procedures to assess the risks of material misstatement of the 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
April 1, 2019

We have served as the Company's auditor since 2018.

LogicBio Therapeutics, Inc.

Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2018	December 31, 2017
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 80,906	$ 24,575
Prepaid expenses and other current assets	1,268	1,118
Total current assets	82,174	25,693
Property and equipment, net	590	232
Restricted cash	146	—
Other assets	—	249
TOTAL ASSETS	$ 82,910	$ 26,174
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Accounts payable	$ 1,168	$ 1,112
Accrued expenses and other current liabilities	1,517	599
Total current liabilities	2,685	1,711
Total liabilities	2,685	1,711
COMMITMENTS AND CONTINGENCIES (Note 12)		
Series A convertible preferred stock, par value of $0.0001 per share; 0 shares and 3,645,848 shares authorized as of December 31, 2018 and December 31, 2017, respectively; 0 shares and 2,976,190 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively; liquidation and redemption value of $0 and $5,137 as of December 31, 2018 and December 31, 2017, respectively	—	4,359
Series B convertible preferred stock, par value of $0.0001 per share; 0 shares and 30,063,791 shares authorized as of December 31, 2018 and December 31, 2017, respectively; 0 shares and 19,541,465 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively; liquidation and redemption value of $0 and $30,428 as of December 31, 2018 and December 31, 2017, respectively	—	28,703
STOCKHOLDERS' EQUITY (DEFICIT):		
Common stock, par value of $0.0001 per share; 175,000,000 and 45,493,828 shares authorized as of December 31, 2018 and December 31, 2017, respectively; 22,188,393 and 1,606,360 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively	3	1
Additional paid-in capital	107,473	1,035
Accumulated other comprehensive loss	(9)	(14)
Accumulated deficit	(27,242)	(9,621)
Total stockholders' equity (deficit)	80,225	(8,599)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)	$ 82,910	$ 26,174

See notes to consolidated financial statements.

LogicBio Therapeutics, Inc.

Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31,	
	2018	2017
OPERATING EXPENSES:		
Research and development	$ 11,079	$ 3,558
General and administrative	6,864	2,296
Total operating expenses	17,943	5,854
LOSS FROM OPERATIONS	(17,943)	(5,854)
OTHER INCOME, NET:		
Interest income, net	567	54
Other (expense) income, net	(159)	67
Total other income, net	408	121
Loss before income taxes	(17,535)	(5,733)
Income tax provision	(86)	(62)
Net loss	$ (17,621)	$ (5,795)
Net loss attributable to common stockholders—basic and diluted (Note 11)	$ (17,621)	$ (7,735)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.04)	$ (5.54)
Weighted-average common stock outstanding—basic and diluted	5,801,533	1,395,381

See notes to consolidated financial statements.

LogicBio Therapeutics, Inc.

Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,	
	2018	2017
Net loss	$(17,621)	$(5,795)
Other comprehensive income (loss):		
Foreign currency translation adjustment	$ 5	$ (14)
Comprehensive loss	$(17,616)	$(5,809)

See notes to consolidated financial statements.

LogicBio Therapeutics, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share data)

	Convertible Preferred Stock									
	Convertible Preferred Stock $0.0001 Par Value Series A		Convertible Preferred Stock $0.0001 Par Value Series B		Common Stock $0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
BALANCE, January 1, 2017	2,976,190	$ 4,359	—	$ —	978,881	$ 1	$ 628	$ —	$ (3,879)	$ (3,250)
Issuance of Series B convertible preferred stock, net of issuance costs of $478	—	—	19,541,465	28,703	—	—	—	—	—	—
Adoption of ASU 2018-07	—	—	—	—	—	—	(53)	—	53	—
Vesting of restricted stock	—	—	—	—	627,479	—	—	—	—	—
Foreign currency translation adjustment	—	—	—	—	—	—	—	(14)	—	(14)
Stock-based compensation expense	—	—	—	—	—	—	460	—	—	460
Net loss	—	—	—	—	—	—	—	—	(5,795)	(5,795)
BALANCE, December 31, 2017	2,976,190	$ 4,359	19,541,465	$ 28,703	1,606,360	$ 1	$ 1,035	$ (14)	$ (9,621)	$ (8,599)
Issuance of common stock to Stanford	—	—	—	—	56,097	—	—	—	—	—
Vesting of restricted stock	—	—	—	—	656,944	—	—	—	—	—
Exercise of options	—	—	—	—	29,217	—	20	—	—	20
Issuance of Common stock upon initial public offering, net of issuance costs of $2,611	—	—	—	—	8,050,000	1	72,253	—	—	72,254
Conversion of Series A preferred shares upon initial public offering	(2,976,190)	(4,359)	—	—	1,558,271	—	4,359	—	—	4,359
Conversion of Series B preferred shares upon initial public offering	—	—	(19,541,465)	(28,703)	10,231,504	1	28,702	—	—	28,703
Foreign currency translation adjustment	—	—	—	—	—	—	—	5	—	5
Stock-based compensation expense	—	—	—	—	—	—	1,104	—	—	1,104
Net loss	—	—	—	—	—	—	—	—	(17,621)	(17,621)
BALANCE, December 31, 2018	—	$ —	—	$ —	22,188,393	$ 3	$ 107,473	$ (9)	$ (27,242)	$ 80,225

See notes to consolidated financial statements.

LogicBio Therapeutics, Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2018	**2017**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$(17,621)	$ (5,795)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	89	43
Loss on disposal of property and equipment	140	—
Stock-based compensation expense	1,104	460
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(150)	(1,032)
Other non-current assets	249	(249)
Accounts payable	35	771
Accrued expenses and other current liabilities	887	20
Net cash used in operating activities	(15,267)	(5,782)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of property and equipment	(614)	(36)
Dispsosal of property and equipment	35	—
Net cash used in investing activities	(579)	(36)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock from the initial public offering	74,865	—
Proceeds from issuance of Series B preferred stock	—	29,181
Payment of issuance costs	—	(478)
Proceeds from exercise of stock options	20	—
Payment of initial public offering costs	(2,579)	—
Net cash provided by financing activities	72,306	28,703
Effect on foreign exchange rates on cash and cash equivalents	17	(38)
NET INCREASE IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH	56,477	22,847
Cash, cash equivalents and restricted cash at beginning of year	24,575	1,728
Cash, cash equivalents and restricted cash at end of year	$ 81,052	$24,575
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Cash paid for interest	$ —	$ 14
Cash paid for taxes	$ 164	$ 4
Property and equipment purchases in accounts payable and accrued expenses	$ 20	$ —
Initial public offering costs in accounts payable and accrued expenses	$ 32	$ —
Conversion of preferred stock to common stock from the initial public offering	$ 33,062	$ —

See notes to consolidated financial statements.

LogicBio Therapeutics, Inc.

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

1. NATURE OF BUSINESS AND BASIS OF PRESENTATION

LogicBio Therapeutics, Inc. ("LogicBio" or the "Company") was incorporated in 2014 as a Delaware corporation. Its principal offices are in Cambridge, Massachusetts. The Company is a genome editing company focused on developing medicines to durably treat rare diseases in patients with significant unmet medical need, using GeneRide, its proprietary technology platform. GeneRide technology is designed to precisely and stably integrate corrective genes into a patient's genome to provide a durable therapeutic effect. The Company has demonstrated proof of concept of its therapeutic platform in animal models for a number of diseases and is focusing on its lead product candidate, LB-001, for the treatment of Methylmalonic Acidemia, a life-threatening disease that presents at birth.

Since its inception, the Company has devoted the majority of its efforts to business planning, research and development, developing markets, raising capital, recruiting management and technical staff. The Company is subject to a number of risks similar to those of other companies conducting high-risk, early-stage research and development of product candidates. Principal among these risks are a dependency on key individuals and intellectual property, competition from other products and companies, and the technical risks associated with the successful research, development and clinical manufacturing of its product candidates. The Company's success is dependent upon its ability to continue to raise additional capital in order to fund ongoing research and development, meet its obligations and, ultimately, obtain regulatory approval of its products, successfully commercialize its products, generate revenue and, attain profitable operations.

On October 23, 2018, the Company completed an initial public offering ("IPO") in which the Company issued and sold 8,050,000 shares of its common stock, including 1,050,000 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $10.00 per share, for aggregate gross proceeds of $80,500. The Company received approximately $72,300 in net proceeds after deducting underwriting discounts and commissions and offering costs.

Upon the closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 11,789,775 shares of common stock at the applicable conversion ratio then in effect. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

Management believes that the Company's existing cash and cash equivalents will allow the Company to continue its operations through 2020. In the absence of a significant source of recurring revenue, the continued viability of the Company beyond that point is dependent on its ability to continue to raise additional capital to finance its operations. There can be no assurance that the Company will be able to obtain sufficient capital to cover its costs on acceptable terms, if at all.

The accompanying consolidated financial statements have been prepared by the Company in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Principles of Consolidation

In January 2016, the Company formed LogicBio Research, LTD ("LogicBio Research"), a wholly owned Israeli subsidiary, for the purpose of conducting research and development activities on the Company's behalf. On September 30, 2018, all operations ceased for LogicBio Research. In April 2018, the Company formed LogicBio Australia Pty Limited ("LogicBio Australia"), a wholly owned Australian subsidiary, for the purpose of

conducting research and development activities on the Company's behalf. In December 2018, the Company formed LogicBio Securities Corporation, which is a Delaware subsidiary created to buy, sell and hold securities. The accompanying consolidated financial statements include the accounts of the Company, LogicBio Research, LogicBio Australia and LogicBio Securities Corporation. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, useful lives assigned to property and equipment, the fair values of common and convertible preferred stock, stock-based compensation and income taxes. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Fair Value Measurements

Certain assets and liabilities are reported on a recurring basis at fair value. 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 and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Cash and Cash Equivalents

Cash and cash equivalents consist of standard checking accounts, money market accounts and a sweep account. The Company considers all highly liquid investments with an original maturity of 90 days or less at the date of purchase to be cash equivalents.

The Company's cash equivalents, which are funds held in money market accounts and a sweep account, are measured at fair value on a recurring basis. As of December 31, 2018 and 2017, the carrying amount of cash equivalents was $80,043 and $24,415, respectively, which approximates fair value and was determined based upon Level 1 inputs. These accounts are valued using quoted market prices with no valuation adjustments applied and are categorized as Level 1.

Concentrations of Credit Risk

Financial instruments that potentially subject us to significant concentration of credit risk consist primarily of cash and cash equivalents. Periodically, the Company may maintain deposits in financial institutions in excess of

government insured limits. The Company believes that it is not exposed to significant credit risk as our deposits are held at financial institutions that management believes to be of high credit quality and the Company has not experienced any losses on these deposits. As of December 31, 2018 and 2017, the Company's cash and cash equivalents were held with two financial institutions. The Company believes that the market risk arising from its holdings of these financial instruments is mitigated based on the fact that many of these securities are either government backed or of high credit rating.

Restricted Cash

As of December 31, 2018, the Company had restricted cash of $146, which represents certificates of deposit serving as collateral for the Company's facility lease. This cash is classified as a non-current asset in the accompanying consolidated balance sheet. The Company did not have restricted cash as of December 31, 2017.

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' (deficit) equity as a reduction of proceeds generated as a result of the offering. Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statement of operations. Upon the closing of the IPO in October 2018, related deferred offering costs were recorded as a reduction to shareholders' equity. As of December 31, 2018, the Company did not have any deferred offering costs recorded.

Property and Equipment

Property and equipment are recorded at cost. Expenditures for repairs and maintenance are expensed as incurred. When assets are retired or disposed of, the assets and related accumulated depreciation are derecognized from the accounts, and any resulting gain or loss is included in the determination of net loss. Depreciation is provided using the straight-line method over the estimated useful lives of the related assets as follows:

	Estimated Useful Life
Computer equipment and software	3 years
Laboratory equipment	5 years
Office furniture	5 years
Leasehold improvements	lesser of useful life or remaining lease term

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceed the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell. To date, no impairments have been recognized for these assets.

Guarantees and Indemnifications

As permitted under Delaware law, the Company indemnifies its officers, directors, consultants and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through December 31, 2018, the Company had not experienced any losses related to these indemnification

obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related liabilities have been established.

Research and Development Costs

Research and development costs are charged to expense as incurred. Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our product candidates, and include:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- license maintenance fees and milestone fees incurred in connection with various license agreements;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and eventually clinical trial materials;
- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, as well as investigative sites, academic institutions and consultants that conduct our preclinical studies and other scientific development services;
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses; and
- costs related to compliance with regulatory requirements.

Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its vendors. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid expenses or accrued expenses and other current liabilities.

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. For the years ended December 31, 2018 and 2017, accumulated comprehensive loss included $9 and $14, respectively, of foreign currency translation adjustments.

Foreign Currency Transactions

The functional currency for the Company's wholly owned foreign subsidiary, LogicBio Australia, is the U.S. Dollar. The functional currency for the Company's wholly owned foreign subsidiary, LogicBio Research, is the Israeli new shekel. Assets and liabilities of LogicBio Research are translated into United States dollars at the exchange rate in effect on the consolidated balance sheet date. Income items and expenses are translated at the average exchange rate in effect during the period. Stockholders' equity (deficit) amounts are translated based on historical exchange rates as of the date of each transaction. Unrealized translation gains and losses are recorded as a foreign currency translation adjustment, which is included in the consolidated statements of convertible preferred stock and stockholder's equity (deficit) as a component of accumulated other comprehensive loss. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in other (expense) income, net in the consolidated statements of operations as incurred.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is made available for evaluation by the chief operating decision maker ("CODM") in making decisions regarding resource allocation and assessing performance. The CODM is the Company's Chief Executive Officer. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular concentration is focused on the development and commercialization of specific genome editing and integration of the therapeutic transgene, utilizing the body's own native processes to drive durable expression.

Common Stock Valuation Prior to the IPO

For the year ended December 31, 2017 and through the consummation of the IPO, due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the estimated fair value of the common stock as of the measurement date. The estimated fair value of the common stock has been determined at each grant date based upon a variety of factors, including:

- the prices at which the Company sold shares of convertible preferred stock and the superior rights and preferences of the convertible preferred stock relative to its common stock at the time of each grant;
- the progress of the Company's research and development programs, including the status and results of preclinical studies for its product candidates;
- the Company's stage of development and commercialization and its business strategy;
- external market conditions affecting the biotechnology industry and trends within the biotechnology industry;
- the Company's financial position, including cash on hand, and its historical and forecasted performance and operating results;
- the lack of an active public market for the Company's common stock and convertible preferred stock;
- the likelihood of achieving a liquidity event, such as an IPO or sale of the Company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biotechnology industry.

Significant changes to the key assumptions underlying the factors used could have resulted in different fair values of common stock at each valuation date.

Convertible Preferred Stock

As of December 31, 2018, the Company did not have any convertible preferred stock ("preferred stock") outstanding. The Company had classified preferred stock as temporary equity in the accompanying consolidated balance sheets due to terms that allowed for redemption of the shares upon certain change in control events that were outside of the Company's control, including sale or transfer of control of the Company as holders of the preferred stock could have caused redemption of the shares in those situations. The Company did not accrete the carrying values of the preferred stock to the redemption values since a liquidation event was not considered probable as of December 31, 2017. Subsequent adjustments of the carrying values to the ultimate redemption values were made only when it became probable that such a liquidation event would occur.

Stock-Based Compensation

The Company accounts for all stock-based payment awards granted to employees and non-employees as stock-based compensation expense at fair value. The Company's stock-based payments include stock options and

grants of common stock, including common stock subject to vesting. The measurement date for employee awards is the date of grant, and stock-based compensation costs are recognized as expense over the employees' requisite service period, which is the vesting period, on a straight-line basis. Prior to the adoption of Accounting Standards Update ("ASU") No. 2018-07, "Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting" ("ASU No. 2018-07"), as discussed below under "Recently Adopted Accounting Pronouncements," the measurement date for non-employee awards was generally the date the services were completed, resulting in financial reporting period adjustments to stock-based compensation during the vesting terms for changes in the fair value of the awards. After the adoption of ASU No. 2018-07, the measurement date for non-employee awards is the later of the adoption date of ASU No. 2018-07 or the date of grant, without changes in the fair value of the award. Stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis. The Company has also issued restricted stock with performance-based vesting conditions and would have recorded the expense for these awards if the Company had concluded that it was probable that the performance condition would be achieved. Stock-based compensation is classified in the accompanying statements of operations based on the function to which the related services are provided. The Company recognizes stock-based compensation expense for the portion of awards that have vested. Forfeitures are accounted for 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. The Company has historically 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. The expected term of the Company's stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Prior to the adoption of ASU No. 2018-07, the expected term for stock options granted to non-employees was equal to the contractual term of the options. After the adoption of ASU No. 2018-07, the expected term of stock options granted to non-employees is determined in the same manner as stock options granted to employees. 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 on common stock and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's consolidated financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that these assets may not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method,

which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's preferred stock contains participation rights in any dividend paid by the Company and is deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares are allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if-converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average number of common shares included in the computation of diluted net loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and preferred stock.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares 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 May 2014, the FASB issued Accounting Standards Update ("ASU") No. 2014-09, "Revenue from Contracts with Customers (Topic 606) (ASU No. 2014-09)," which modifies how all entities recognize revenue, and consolidates into one ASC (ASC Topic 606, Revenue from Contracts with Customers) the current guidance found in ASC Topic 605, and various other revenue accounting standards for specialized transactions and industries. ASU No. 2014-09 outlines a comprehensive five-step revenue recognition model based on the principle that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU No. 2014-09 may be applied using either a full retrospective approach, under which all years included in the financial statements will be presented under the revised guidance, or a modified retrospective approach, under which financial statements will be prepared under the revised guidance for the year of adoption, but not for prior years. Under the latter method, entities will recognize a cumulative catch-up adjustment to the opening balance of retained earnings at the effective date for contracts that still require performance by the entity at the date of adoption. In August 2015, the FASB issued ASU No. 2015-14, "Revenue from Contracts with Customers (Topic 606): Deferral of Effective Date (ASU No. 2015-14)," which defers the effective date of ASU No. 2014-09 by one year. The guidance is effective for the Company for annual reporting periods beginning after December 15, 2017. To date, the Company has not had any arrangements that are within the scope of ASU No. 2014-09, or its predecessor, ASC Topic 605. The Company adopted these pronouncements effective January 1, 2017. The adoption of ASU No. 2014-09 did not have any impact on the Company's consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Improvements to Employee Share-Based Payment Accounting ("ASU No. 2016-09"), which simplifies share-based payment accounting through a variety of amendments. The Company elected to early adopt this guidance effective January 1, 2016 and has elected to account for forfeitures as incurred and therefore no forfeiture estimate is utilized in the twelve months ended December 31, 2016. The adoption of ASU No. 2016-09 did not have a material impact on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, "Statement of Cash Flows (Topic 230): Restricted Cash." ASU No. 2016-18 provides guidance on the classification and presentation of changes in restricted

cash and cash equivalents in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years, with early adoption permitted. The Company adopted this guidance effective January 1, 2018. Adoption of ASU No. 2016-18 did not have a material impact on the Company's consolidated financial statements.

In May 2017, the FASB issued ASU No. 2017-09, "Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting," 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 standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted. The Company adopted this guidance effective January 1, 2018. The implementation of ASU 2017-09 did not have a material effect on the Company's consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, "Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting." These amendments expand the scope of Topic 718, Compensation—Stock Compensation (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. The ASU supersedes Subtopic 505-50, Equity—Equity-Based Payments to Non-Employees. This standard is effective for public companies for annual periods beginning after December 15, 2018, including interim periods within those fiscal years, with early adoption permitted as long as ASU No. 2014-09 has been adopted by the Company. The Company adopted this guidance effective January 1, 2017. The adoption of ASU No. 2018-07 did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, "Leases (Topic 842)," which requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases. The ASU will also require new qualitative and quantitative disclosures to help investors and other financial statement users better understand the amount, timing, and uncertainty of cash flows arising from leases. ASU No. 2016-02 is effective for fiscal years beginning after December 15, 2018, with early adoption permitted. In July 2018, an amendment was made that allows companies the option of using the effective date of the new standard as the initial application date (at the beginning of the period in which it is adopted, rather than at the beginning of the earliest comparative period). The standard is effective for the Company on January 1, 2019. The Company has completed its assessment on the impact of the standard, including optional practical expedients and transition methods that the Company will elect upon adoption. The implementation plan included identifying the Company's lease population, assessing significant leases under the new guidance and identifying changes to processes and controls. The Company concluded that upon adoption of this standard there will not be a material impact on the Company's consolidated financial statements.

3. FAIR VALUE MEASUREMENTS

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

Description	December 31, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets				
Sweep bank account	$ 831	$ 831	$ —	$ —
Money market funds	$ 79,212	$ 79,212	$ —	$ —
Total financial assets	$ 80,043	$ 80,043	$ —	$ —

Description	December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets				
Sweep bank account	$ 24,415	$ 24,415	$ —	$ —
Total financial assets	$ 24,415	$ 24,415	$ —	$ —

There have been no transfers between fair value measure levels during the years ended December 31, 2018 and 2017.

4. PROPERTY AND EQUIPMENT, NET

Property and equipment, net consisted of the following:

	December 31, 2018	December 31, 2017
Computer equipment and software	$ 36	$ 23
Laboratory equipment	582	264
Office furniture	21	7
Total	639	294
Less: Accumulated depreciation	(49)	(62)
Property and equipment, net	$ 590	$ 232

Depreciation expense for the years ended December 31, 2018 and 2017 was $89 and $43, respectively. Maintenance and repairs are charged to expense as incurred and any additions or improvements are capitalized.

5. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities at December 31, 2018 and 2017 consisted of the following:

	December 31, 2018	December 31, 2017
Accrued compensation and benefits	$ 709	$ 290
Accrued insurance	—	20
Accrued professional services	585	64
Other	223	225
Total accrued expenses and other current liabilities	$ 1,517	$ 599

Accrued compensation and benefits consists primarily of accrued bonuses, accrued commissions, and accrued vacation. Accrued professional services consists primarily of consulting services and legal services.

6. LICENSE AGREEMENTS

In December 2015, the Company entered into a license agreement (the "Stanford Agreement") with The Board of Trustees of the Leland Stanford Junior University ("Stanford"), a private research university, pursuant to which the Company obtained an exclusive, worldwide license to make, have made, use, import, offer to sell and sell products covered by certain patent rights to the GeneRide technology owned by Stanford within certain fields of use. As consideration for the license, the Company paid a one-time, non-refundable license fee and issued shares of common stock. The Company also agreed to pay for certain patent expenses per the terms of the Stanford Agreement. The license term extends indefinitely, unless terminated earlier by either party under certain provisions. The Company is required to pay annual license fees.

The Company is also required to reimburse Stanford for additional patent costs incurred, pay amounts up to approximately $1,300 upon achievement of certain development and commercialization milestones, pay royalties on future sales as a low single-digit percentage of net sales and royalties on sublicensing revenue as a low double-digit percentage of net sales, if any. The Company is required to pay Stanford a fee of $325 in the event of a change of control. The Company recorded research and development expense related to the Stanford Agreement of $131 and $40 in the years ended December 31, 2018 and 2017, respectively. The Company has paid a total of $298 to Stanford through December 31, 2018.

In May 2018, the Company entered into a license agreement (the "UT Agreement") with The University of Texas System ("UT"), pursuant to which the Company obtained an exclusive, worldwide license to manufacture, have manufactured, distribute, have distributed, use, offer for sale, sell, lease, loan or import products covered by certain patent rights to the GeneRide technology owned by UT (jointly with Stanford) within certain fields of use. As consideration for the license, the Company paid a one-time, non-refundable license fee of $25, which will be recorded as research and development expense. The Company also agreed to pay an annual license maintenance fee, which is creditable against royalties owed the same year the maintenance fee is paid. The Company is also obligated to reimburse UT for expenses associated with the prosecution and maintenance of the UT patent rights. UT is entitled to receive clinical and regulatory milestone payments upon the first occurrence of specified milestone events and the Company is obligated to make additional payments to UT of up to $3,000 upon the first occurrence of certain sales milestones. UT is also entitled to receive royalties on net sales of licensed products ranging from below single-digit to low single-digit percentage royalties on net sales. The Company recorded $25 as research and development expense in the year ended December 31, 2018. The Company has paid a total of $30 to this institution through December 31, 2018

In November 2018, LogicBio Australia entered into a collaboration and license agreement (the "CMRI Agreement") with Children's Medical Research Institute ("CMRI"), a private research institution, pursuant to

which LogicBio Australia and CMRI will work together to develop new viral vectors over a two-year period from the effective date of the CMRI Agreement ("Research Term"). Pursuant to the CMRI Agreement, LogicBio Australia obtained an exclusive, worldwide license to make, have made, use, import, offer to sell and sell products covered by certain patent rights to the new viral vectors. As consideration for the license, LogicBio Australia will pay to CMRI royalties in the low single digits and certain milestone payments. In addition to the consideration for the license, LogicBio Australia will pay research funds to CMRI during the Research Term of $2.0 million over the term of the CMRI Agreement.

In December 2018, the Company entered into a license agreement (the "NIH Agreement") with the NIH ("the NIH"), pursuant to which the Company obtained a non-exclusive, worldwide license under certain specified patent rights relating to a synthetic codon-optimized MUT gene that is incorporated into the LB-001 GeneRide construct, to exploit products and practice processes that are covered by the licensed patent rights in the field of research, development, manufacture and commercialization of pharmaceutical products for the treatment or prevention of MMA using gene therapy constructs in humans. As consideration for the license, NIH is entitled to receive an upfront payment of $25, and payments of up to an aggregate of approximately $9,700 upon the achievement of certain specified development, regulatory and sales-based benchmarks. The NIH is also entitled to receive running royalties on annual net sales of licensed products at certain low- to mid-single digit royalty rates, which rates vary based on the geographic market in which a sale occurs.

Any potential future milestone or royalty payment amounts have not been accrued at December 31, 2018 due to the uncertainty related to the successful achievement of these milestones.

7. CONVERTIBLE PREFERRED STOCK

On January 6, 2016, the Company authorized the sale and issuance of up to 3,645,848 shares of Series A convertible preferred stock ("Series A Preferred Stock") at a par value of $0.0001. On January 13, 2016, the Company issued 2,678,571 shares of Series A Preferred Stock at $1.4933 per share for gross proceeds of $4,000. Issuance costs were $85. On March 21, 2016, the Company issued 297,619 shares of Series A Preferred Stock at $1.4933 per share for gross proceeds of $444.

On June 19, 2017, the Company authorized the sale and issuance of up to 30,063,791 shares of Series B convertible preferred stock ("Series B Preferred Stock") at a par value of $0.0001. The Series B Preferred Stock financing was structured to close in two tranches. The first tranche closed on June 19, 2017, with the issuance of 19,541,465 shares of Series B Preferred Stock at $1.4933 per share for gross proceeds of $29,181. Issuance costs were $478. The second tranche closing is contingent upon the achievement or waiver of a certain regulatory milestone event ("Milestone Event"). The additional shares of Series B Preferred Stock to be issued upon achievement or waiver of the Milestone Event total 10,522,281 shares at $1.4933 per share for gross proceeds of $15,713.

Series A Preferred Stock and Series B Preferred Stock is collectively referred to as "Preferred Stock."

On October 23, 2018, upon the closing of the Company's IPO, all outstanding shares of Preferred Stock converted into 11,789,775 shares of the Company's common stock. As such, there were no outstanding shares of Preferred Stock as of December 31, 2018. As of December 31, 2017, Preferred Stock consisted of the following:

	December 31, 2017				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Value	Common stock Issuable Upon Conversion
Series A Preferred Stock	3,645,848	2,976,190	$ 4,359	$ 5,137	1,558,271
Series B Preferred Stock	30,063,791	19,541,465	28,703	30,428	10,231,504
	33,709,639	22,517,655	$33,062	$ 35,565	11,789,775

The rights and privileges of the preferred stockholders were as follows:

Conversion: Each share of Preferred Stock was convertible, at the option of the holder, at any time, into shares of common stock on a one-for-1.90993 basis. The conversion ratio was determined by dividing the original issue price of $1.4933 by the conversion price of $0.78186. The Preferred Stock would automatically convert into shares of common stock at the closing a Qualified IPO (as defined in the Company's Amended and Restated Certificate of incorporation, as amended from time to time) or in a non-Qualified IPO, upon the approval of at least 60% of the Preferred Stockholders.

Liquidation Preference: Prior to the IPO, in the event of any liquidation or "Deemed Liquidation Event," defined below, the preferred stockholders would have been entitled to the greater of (i) the original issue price of the Preferred Stock plus any accrued dividends not yet paid plus any other dividends declared and unpaid or (ii) the amount payable had all classes of shares been converted to common stock. In the event of a Deemed Liquidation Event, accrued dividends would not exceed 40% of the original issue price. After payments of all preferential amounts are made to the Preferred Stockholders, any remaining assets would be distributed to the common stockholders on a pro rata basis. A Deemed Liquidation Event was defined as a merger, consolidation, reorganization or similar transaction; the sale transfer, exclusive license of all or substantially all of the Company's assets/intellectual property; or the sale or transfer of shares to any person (or group of related or affiliated persons), directly or indirectly, representing a greater than 50% of the voting power of the voting securities of the Company.

Dividends: Preferred stockholders were entitled to receive, when and if declared by the Board out of any funds legally available, dividends at the rate of 8% of the original issue price per share. No dividends were declared or paid through October 23, 2018, the date on which all of the Company's preferred stock was converted to common stock upon the closing of the Company's IPO.

Voting Rights: Preferred Stock and common stock voted together as one class on an as converted basis.

8. COMMON STOCK

As of December 31, 2018, and 2017, the Company's certificate of incorporation authorized the Company to issue 175,000,000 shares and 45,493,828 shares, respectively, of $0.0001 par value common stock.

The following is a summary of the rights and privileges of the holders of common stock as of December 31, 2018:

Voting: Each holder of common stock shall be entitled to one vote for each share of common stock held of record by such holder on all matters on which stockholders generally are entitled to vote.

Dividends: Dividends of cash or property may be declared and paid on the common stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend rights of any then outstanding Preferred Stock. The holders of record of common stock shall share ratably in all dividends payable in cash, stock or otherwise and other distributions, whether in respect of liquidation or dissolution (voluntary or involuntary) or otherwise. As of December 31, 2018, no dividends have been declared or paid.

Liquidation Rights: Upon the dissolution, liquidation or winding up of the affairs of the Company, whether voluntary or involuntary, after payment or provision for payment of the debts and liabilities of the Company and of the preferential and other amounts, if any, to which the holders of Preferred Stock shall be entitled, holders of common stock shall be entitled to receive all assets of the Company available for distribution to its stockholders, ratably in proportion to the number of shares held by each such stockholder. A merger or consolidation of the Company with or into any other corporation or other entity or a sale or conveyance of all or any part of the assets

of the Company, in any such case that does not in fact result in the liquidation of the Company and the distribution of assets to its stockholders, shall not be deemed to be a voluntary or involuntary liquidation or dissolution or winding up of the Company.

In July 2018, the Company issued 56,097 shares of common stock to Stanford, pursuant to the anti-dilution right under the Stanford Agreement.

In October 2018, the Company completed an initial public offering in which the Company issued and sold 8,050,000 shares of its common stock, including 1,050,000 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $10.00 per share, for aggregate gross proceeds of $80,500. The Company received approximately $72,300 in net proceeds after deducting underwriting discounts and commissions and offering costs. In connection with this financing, all outstanding shares of Preferred Stock converted into 11,789,775 shares of the Company's common stock.

As of December 31, 2018 and 2017, the Company has reserved the following shares of common stock for the potential conversion of outstanding Preferred Stock and exercise of stock options:

	December 31, 2018	December 31, 2017
Preferred Stock	—	11,789,775
Options to purchase common stock	2,702,747	1,454,709
Total	2,702,747	13,244,484

9. STOCK-BASED COMPENSATION

Equity Incentive Plans

In December 2014, the Company adopted the LogicBio Therapeutics, Inc. 2014 Equity Compensation Plan (the "2014 Plan") for the issuance of stock options and other stock-based awards.

In October 2018, the Company's 2018 Equity Incentive Plan (the "2018 Plan") became effective, and as a result no further awards will be made under the 2014 Plan. The 2018 Plan was established to provide equity-based ownership opportunities for employees and directors, as well as outside consultants and advisors. The 2018 Plan authorized up to 1,183,214 of shares of the Company's common stock to be issued. At December 31, 2018, there were 477,924 shares available for future grant under the 2018 Plan. In addition, any previously granted awards under the 2014 Plan will remain outstanding in accordance with their respective terms.

Under the 2018 Plan, there is an annual increase on January 1 of each year from 2019 until 2028, by the lessor of (i) 4% of the number of shares of common stock outstanding on December 31 of the prior year, and (ii) an amount determined by the Board.

The 2014 Plan and the 2018 Plan are collectively referred to as the "Plans".

The Plans are administered by the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of stock 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 Plans expire 10 years after the grant date, unless the board of directors sets a shorter term. Vesting periods for awards under the Plans are determined at the discretion of the board of directors. Incentive stock options granted to employees and shares of restricted stock granted to employees, officers, members of the board of directors, advisors, and consultants of the Company typically vest over four years. Non-statutory options and shares of restricted stock granted to employees, officers, members of the board of directors, advisors, and consultants of the Company typically vest over three or four years.

The Company recorded stock-based compensation expense for options granted of $801 and $255 during the years ended December 31, 2018 and 2017, respectively. The Company recorded stock-based compensation expense for restricted stock granted of $303 and $205 during the years ended December 31, 2018 and 2017, respectively.

Stock Option Valuation

The assumptions that the Company used in Black-Scholes options pricing model to determine the grant-date fair value of stock options granted to employees and non-employees for the years ended December 31, 2018 and 2017 were as follows:

	Year Ended December 31,	
	2018	2017
Weighted-average risk-free interest rate	2.91%	2.11%
Expected term (in years)	5.92	5.92
Expected volatility	70.03%	69.19%
Expected dividend yield	0.00%	0.00%

Stock Options

A summary of option activity under the Plans during the year ended December 31, 2018 is as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2017	1,454,709	$ 0.73	9.83	$ 3
Granted	1,301,684	5.78		—
Exercised	(29,217)	0.69		202
Cancelled or forfeited	(24,429)	—		—
Outstanding as of December 31, 2018	2,702,747	$ 3.16	9.21	$ 19,591
Options exercisable as of December 31, 2018	812,429	$ 0.93	8.86	$ 7,697
Options unvested as of December 31, 2018	1,890,318	$ 4.12	9.36	$ 11,894

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock.

The weighted-average grant date fair value per share of options granted during the years ended December 31, 2018 and 2017 was $5.46 and $0.44, respectively. As of December 31, 2018 and 2017, there was $6,680 and $380, respectively, of unrecognized stock-based compensation expense related to unvested employee and non-employee stock options. The unrecognized stock-based compensation expense is estimated to be recognized over a period of 2.5 and 2.4 years at December 31, 2018 and 2017, respectively.

The total fair value of options vested during the years ended December 31, 2018 and 2017 was $232 and $243, respectively.

Shares of Restricted Common Stock

The Company has granted shares of restricted common stock with time-based and performance-based vesting conditions. A summary of restricted stock activity under the Plans during the year ended December 31, 2018 is as follows:

	Restricted Stock	Weighted-Average Grant Date Fair Value
Unvested as of December 31, 2017	1,434,610	$ 0.27
Granted	107,054	4.02
Vested or Released	(656,944)	2.50
Unvested as of December 31, 2018	884,720	$ 0.63

The weighted-average grant date fair value per share of restricted stock granted during the years ended December 31, 2018 and 2017 was $4.02 and $0.71, respectively. As of December 31, 2018 and 2017, there was $529 and $398, respectively, of unrecognized stock-based compensation expense related to unvested employee and non-employee restricted stock. The unrecognized stock-based compensation expense is estimated to be recognized over a period of 0.9 and 1.8 years at December 31, 2018 and 2017, respectively.

The total fair value of restricted stock vested during the years ended December 31, 2018 and 2017 was $160 and $156, respectively.

Stock-Based Compensation Expense

Total stock-based compensation expense recorded as research and development and general and administrative expenses, respectively, for employees, directors and non-employees during the years ended December 31, 2018 and 2017 is as follows:

	Year Ended December 31,	
	2018	2017
Research and development	$ 284	$374
General and administrative	820	86
Total stock-based compensation expense	$1,104	$460

10. INCOME TAXES

During the years ended December 31, 2018 and 2017, the Company recorded full valuation allowance on federal and state deferred balances since management does not forecast the Company to be in a profitable position in the near future.

Loss before the provision for income taxes for the years ended December 31, 2018 and 2017 consisted of the following:

	Year Ended December 31,	
	2018	2017
United States	$(17,284)	$(5,832)
Foreign	(337)	99
	$(17,621)	$(5,733)

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 taxes, net of federal benefit	2.4	—
Foreign rate differential	0.1	0.2
Research and development tax credits	2.4	—
Meal and entertainment	—	(0.1)
Stock based compensation	(0.7)	(0.3)
Section 965 subpart F	—	(0.2)
Valuation allowances	(25.2)	(25.4)
Rate changes	(0.1)	(21.4)
Other	0.1	—
Effective income tax rate	— %	(13.2)%

Net deferred tax assets as of December 31, 2018 and 2017 consisted of the following:

	December 31,	
	2018	2017
Net operating loss carryforwards	$ 6,089	$ 2,170
Reserves & accruals not currently deductible	324	231
Federal & state credit carryforwards	433	11
Total deferred tax assets	6,846	2,412
Valuation allowance	(6,846)	(2,412)
Net deferred tax assets	$ —	$ —

At December 31, 2018, the Company had available net operating loss carryforwards for federal and state income tax purposes of approximately $25,854 and $9,324, respectively, which if not utilized earlier, will begin to expire in 2037. The Company had federal research credits of approximately $204, which, if not utilized earlier, will begin to expire in 2035, and state research credits of approximately $290.

As of December 31, 2017, the Company had U.S. federal and state net operating loss carryforwards of $8,738 and $3,485, respectively, which may be available to offset future income tax liabilities and begin to expire in 2037. As of December 31, 2017, the Company also had California state research and development tax credit carryforwards of $8. The federal research and development credit had been fully utilized to offset payroll tax credit in 2017.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018 and 2017 related primarily to the increases in net operating loss carryforwards and research and development tax credit carryforwards and were as follows:

	Year Ended December 31,	
	2018	2017
Valuation allowance at beginning of year	$(2,412)	$(1,287)
Increases recorded to income tax provision	(4,443)	(1,125)
Decreases recorded to income tax provision	9	—
Valuation allowance at end of year	$(6,846)	$(2,412)

The Company's U.S. federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2014 through December 31, 2017. There are currently no pending income 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 period. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

11. LOSS PER SHARE

Basic loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding:

	Year Ended December 31,	
	2018	2017
Numerator:		
Net loss	$ (17,621)	$ (5,795)
Less: Accruals of dividends of preferred stock	—	(1,940)
Net loss attributable to common stockholders—basic and diluted	(17,621)	(7,735)
Denominator:		
Weighted-average common stock outstanding	5,801,533	1,395,381
Net loss per share attributable to common stockholders—basic and diluted	$ (3.04)	$ (5.54)

The Company's potential dilutive securities, which include Preferred Stock, restricted stock, and stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares 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 common shares, presented based on amounts outstanding at December 31, 2018 and 2017, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	December 31,	
	2018	2017
Preferred Stock	—	11,789,775
Unvested restricted stock	884,720	1,434,610
Options to purchase common stock	2,702,747	1,454,709

12. COMMITMENTS AND CONTINGENCIES

Operating Leases

In December 2018, the Company entered into an operating lease for laboratory and office space in Cambridge, Massachusetts for a 14-month term, ending in March 2020.

Future minimum lease payments as of December 31, 2018 are as follows:

Year Ending December 31,	
2019	$1,028
2020	223
	$1,251

A letter of credit was established in connection with the facility lease in the amount of $146. As of December 31, 2018, the letter of credit was classified as restricted cash.

Rent expense under the operating lease was $880 and $157 for the years ended December 31, 2018 and 2017, respectively.

Refer to Note 6, License Agreements, for any potential future milestone or royalty payment amounts. These are not currently probable or estimable.

Legal Proceedings

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities.

13. RELATED PARTIES

In January 2016, the Company entered into a consulting agreement with two of its founders, who are also board members. Under the terms of each agreement, the Company will pay an annual fee of $68 to each of these founders. Each founder will provide research and development consulting services to the Company. For the years ended December 31, 2018 and 2017, the Company has made payments to each of these founders of $68. In addition, each founder received $5 for their participation in the Scientific Advisory Board beginning in 2018. Each founder has also received stock options for their services as either as a board member or member of the Scientific Advisory Board.

In March 2017, the Company subleased to an affiliate, certain space in Tel Aviv, Israel, for approximately 15 months. On September 30, 2018, the Company ceased operations in Israel. For the years ended December 31, 2018 and 2017, the Company recognized income of $21 and $41 to other income, net, respectively.

On October 1, 2018, the Company entered into a consulting agreement with one of its founders, who is also a board member. Under the terms of the agreement, the Company will pay an annual fee of $68 to the founder. The founder will provide research and development consulting services to the Company. For the year ended December 31, 2018, the Company has made payments to the founder of $17. In addition, the founder received $5 for his participation in the Scientific Advisory Board beginning in 2018.

14. GEOGRAPHIC INFORMATION

The Company's property and equipment, net by location was as follows:

	December 31, 2018	December 31, 2017
Israel	—	228
United States	$ 590	$ 4
Total property and equipment, net	$ 590	$ 232

15. SUBSEQUENT EVENTS

Research Agreement

In January 2019, the Company entered into letter of intent with a private contract development and manufacturing organization, or CDMO, to cover certain research and development activities (the "LOI"). The CDMO is responsible for the research and development activities under the LOI, which the Company will fund. The Company paid a one-time, non-refundable project initiation fee of $1,000, which will be recorded as research and development expense.

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Exhibit 10.3

PUBLIC HEALTH SERVICE

PATENT LICENSE AGREEMENT NONEXCLUSIVE – SUBLICENSABLE

This **Agreement** is based on the model Patent License Non-Exclusive Sublicensable Agreement adopted by the U.S. Public Health Service ("**PHS**") Technology Transfer Policy Board for use by components of the National Institutes of Health ("**NIH**"), the Centers for Disease Control and Prevention ("**CDC**"), and the Food and Drug Administration ("**FDA**"), which are agencies of the **PHS** within the Department of Health and Human Services ("**HHS**").

This Cover Page identifies the Parties to this **Agreement**:

The U.S. Department of Health and Human Services, as represented by

National Human Genome Research Institute (NHGRI) an Institute

(hereinafter referred to as the "**IC**") of the

NIH

and

LogicBio Therapeutics, Inc.,

hereinafter referred to as the "Licensee", having offices at 610 Main Street, 3rd Floor, Cambridge, MA 02139, created and operating under the laws of Delaware.

Tax ID No.:_47-1514975

[***] Portions of this exhibit have been redacted pursuant to a Confidential Treatment Request. An unredacted version of this exhibit has been filed separately with the Commission.

For the **IC's** internal use only:

License Number:

License Application Number:

Serial Number(s) of Licensed Patent(s) or Patent Application(s):

Licensee:

Cooperative Research and Development Agreement (CRADA) Number (if a subject invention):

Additional Remarks:

Public Benefit(s):

This Patent License Agreement, hereinafter referred to as the "**Agreement**", consists of this Cover Page, an attached **Agreement**, a Signature Page, Appendix A (List of Patent(s) or Patent Application(s)), Appendix B (Fields of Use and Territory), Appendix C (Royalties), Appendix D (Benchmarks), Appendix E (Commercial Development Plan), Appendix F (Example Royalty Report), and Appendix G (Royalty Payment Options).

The **IC** and the **Licensee** agree as follows:

1. BACKGROUND

1.1 In the course of conducting biomedical and behavioral research, the **IC** investigators made inventions that may have commercial applicability.

1.2 By assignment of rights from the **IC** employees and other inventors, **HHS**, on behalf of the **Government**, owns intellectual property rights claimed in any United States or foreign patent applications or patents corresponding to the assigned inventions. **HHS** also owns any tangible embodiments of these inventions actually reduced to practice by the **IC**.

1.3 The Secretary of **HHS** has delegated to the **IC** the authority to enter into this **Agreement** for the licensing of rights to these inventions under 35 U.S.C. §§200-212, the Federal Technology Transfer Act of 1986, 15 U.S.C. §3710(a), and the regulations governing the licensing of Government-owned inventions, 37 CFR Part 404.

1.4 The **IC** desires to transfer these inventions to the private sector through commercialization licenses to facilitate the commercial development of products and processes for public use and benefit.

1.5 The **Licensee** desires to acquire commercialization rights to certain of these inventions in order to develop processes, methods, or marketable products for public use and benefit.

2. DEFINITIONS

2.1 "**Affiliate**" of an entity means any corporation or other business entity controlled by, controlling, or under common control with such entity at any time during the term of the agreement. For this purpose, "control" means direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock or at least fifty percent (50%) interest in the income of the corporation or other business entity.

2.2 "**Australian Orphan Drug Exclusivity**" means exclusive marketing rights granted by the Australian Government's Department of Health, Therapeutic Goods Administration ("TGA"), upon approval of an orphan drug in Australia. Orphan drug designation status granted by the TGA typically gives marketing exclusivity in Australia for 5 years after approval.

2.3 **"Biologics License Application (BLA)**" means a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce (21 CFR 601.2).

2.4 "**Combination Product**" means a product that contains a **Licensed Product** and at least one other active therapeutic component or one other device other than a **Licensed Product**. For the avoidance of doubt, "Combination Products" include products in which a gene therapy product comprises multiple active therapeutic components, including a transgene, a cassette and a capsid.

2.5 "**Effective Date**" means the date set forth in Paragraph 13.1.

2.6 "**European Orphan Drug Exclusivity**" means exclusive marketing rights granted by European Medicines Agency (EMA) upon approval of an orphan drug in European Union. Orphan drug status granted by the EMA gives marketing exclusivity in European Union for 10 years after approval.

2.7 "**FDA**" means the United States Food and Drug Administration.

2.8 "**First Commercial Sale**" means the initial transfer by or on behalf of the **Licensee** or its **Sublicensees** of **Licensed Products** or the initial practice of a **Licensed Process** by or on behalf of the **Licensee** or its **Sublicensees**, in either case, pursuant to a valid marketing authorization from a competent regulatory authority body (for example, NDA approval by FDA in the United States) in exchange for cash or some equivalent to which value can be assigned for the purpose of determining **Net Sales**.

2.9 "**Government**" means the Government of the United States of America.

2.10 "**Japanese Orphan Drug Exclusivity**" means exclusive marketing rights granted by the Japanese Ministry of Health, Labour and Welfare (MHLW) upon approval of an orphan drug in Japan. Orphan drug designation status granted by the MHLW gives marketing exclusivity in Japan for up to 10 years after approval.

2.11 "**Licensed Fields of Use**" means the fields of use identified in Appendix B.

2.12 "Licensed Patent Rights" shall mean:

(a) Patent applications (including provisional patent applications and PCT patent applications) or patents listed in Appendix A, all divisions and continuations of these applications, all patents issuing from these applications, divisions, and continuations, and any reissues, reexaminations, and extensions of all these patents;

(b) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in 2.12(a):

(i) continuations-in-part of 2.12(a);

(ii) all divisions and continuations of these continuations-in-part;

(iii) all patents issuing from these continuations-in-part, divisions, and continuations;

(iv) priority patent application(s) of 2.12(a); and

(v) any reissues, reexaminations, and extensions of all these patents;

(c) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in 2.12(a): all counterpart foreign and U.S. patent applications and patents to 2.12(a) and 2.12(b), including those listed in Appendix A; and

(d) **Licensed Patent Rights** shall *not* include 2.12(b) or 2.12(c) to the extent that they contain one or more claims directed to new matter which is not the subject matter disclosed in 2.12(a).

2.13 "**Licensed Processes**" means processes, which in the course of being practiced, would be within the scope of one or more claims of the **Licensed Patent Rights** that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction.

2.14 "**Licensed Product**" means tangible materials, which in the course of development, manufacture, use, distribution, sale, or importation, would be within the scope of one or more claims of the **Licensed Patent Rights** that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction. For clarity, Licensee shall pay running royalties and benchmark royalties with respect to Licensed Products the development, manufacture, use, distribution, sale or importation of which are no longer within the scope of one or more claims of the Licensed Patents Rights in a country that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction if such products have valid **Orphan Drug Exclusivity** in such country.

2.15 "**Licensed Territory**" means the geographical area identified in Appendix B.

2.16 "**MMA**" means Methylmalonic Acidemia, which is an inherited disorder in which the body is unable to process certain proteins and fats (lipids) properly.

2.17 "**Net Sales**" means the total gross receipts for sales of Licensed Products or practice of Licensed Processes by or on behalf of the Licensee or its Sublicensees, and from leasing, renting, or otherwise making Licensed Products available to others without sale or other dispositions, whether invoiced or not, less returns and allowances, packing costs, insurance costs, freight out, taxes or excise duties imposed on the transaction (if separately invoiced), and wholesaler and cash discounts in amounts customary in the trade to the extent actually granted. No deductions shall be made for commissions paid to individuals, whether they are with independent sales agencies or regularly employed by the Licensee or a **Sublicensee** and on its payroll, or for the cost of collections.

If the **Licensee**, **Affiliates** or its **Sublicensees** sell a **Combination Product**, the **Net Sales** for such **Combination Product** shall be the market price of the **Licensed Product** portion of the **Combination Product** when sold separately, and if the **Licensed Product** is not sold separately, then the **Net Sales** for such **Combination Product** shall be the greater of (i) the market price at which the **Licensed Product** reasonably could be sold as a separate item, or (ii) **Net Sales** of the **Combination Product** multiplied by a factor 1/x, where x is the number of active components and/or devices contained in the **Combination Product**, wherein x cannot exceed a value of five (5).

2.18 "**Orphan Indication**" means a disease that affects less than two hundred thousand (200,000) people in the United States as defined by the **FDA** or five (5) in ten thousand (10,000) people in the European Union as defined by the European Medicines Agency.

2.19 "**Orphan Drug Designation**" means the granting of special status by a country and/or government regulatory agency (such as the FDA, EMA, MHLW, or TGA) to a drug or biological product ("drug") to treat a rare disease or condition upon request of a sponsor under the U.S. Orphan Drug Act (ODA) or any foreign equivalent(s) to this law enacted by other countries including but not limited to Australia, member countries of European Union, and Japan.

2.20 "**Orphan Drug Exclusivity**" means exclusive marketing rights granted by a country and/or government regulatory agency (such as the FDA, EMA, MHLW, or TGA) to a drug or biological product ("drug") to treat a rare and/or neglected disease or condition upon regulatory approval of said drug for a given period of time (which varies from country to country) and which can run concurrently with a patent or not.

2.21 "**Phase 1 Clinical Study**" means the initial introduction of an investigational new drug into humans, the principal purpose of which is to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness, in compliance with 21 C.F.R. §312(a) or foreign equivalent.

2.22 "**Phase 2 Clinical Study**" means controlled human clinical studies conducted to evaluate the effectiveness of a drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug in compliance with 21 C.F.R. §312(b) or foreign equivalent, and shall include any clinical study that leads to a conditional regulatory approval, that is followed by a confirmatory **Phase 3 Clinical Study**.

2.23 "**Phase 3 Clinical Study**" means expanded controlled and uncontrolled human clinical trials pursuant to a randomized study with endpoints agreed upon by regulatory bodies for regulatory approval performed after **Phase 2 Clinical Study** evidence suggesting effectiveness of a drug has been obtained, and is intended to gather additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of a drug and to provide an adequate basis for regulatory approval and physician labeling, as in compliance with 21 C.F.R. §312 or foreign equivalent, and shall include a confirmatory study that is conducted following conditional regulatory approval.

2.24 "**Practical Application**" means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and in each case, under these conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or **Government** regulations available to the public on reasonable terms.

2.25 "**Priority Review**" means, with respect to a human drug application as defined in 21 USC § 379g(l), review and action by the Secretary of **HHS** ("**Secretary**") on such application as described in the Manual of Policies and Procedures of the Food and Drug Administration (FDA) and goals identified in the letters described in Section 101(b) of the Prescription Drug User Fee Amendments of 2012.

2.26 "**Priority Review Voucher**" means a voucher issued by the **Secretary** to the sponsor of a **Rare Pediatric Disease Product Application** that entitles the holder of such voucher to priority review of a single human drug application submitted under 21 USC § 355(b)(1) or Section 351(a) of the Public Health Service Act [42 USC § 262(a)] after the date of approval of the **Rare Pediatric Disease Product Application**.

2.27 "**Rare Pediatric Disease**" means a disease that meets each of the following criteria: **(A)** The disease is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; **(B)** The disease is a rare disease or condition, within the meaning of 21 USC § 360bb.

2.28 "**Rare Pediatric Disease Product Application**" means a human drug application, as defined in 21 USC § 360ff (a)(4), for a **Rare Pediatric Disease**.

2.29 "**Sublicensee**" means a legal entity, which is not an Affiliate of Licensee, which receives a sublicense of some or all of the rights granted to Licensee under this Agreement.

2.30 "**Third Party**" means an entity other than (i) **Licensee** or any of its **Affiliates** or **Sublicensees** and (ii) **IC**.

2.31 "**U.S. Orphan Drug Exclusivity**" means exclusive marketing rights granted by the FDA upon approval of an orphan drug and can run concurrently with a patent or not. The right prevents the submission or effective approval of ANDAs or applications (ANDA, 505(b)(2) or "full" NDA or BLA) for the same drug for the same orphan disease or condition for seven years after FDA approval.

2.32 "**Valid Claim**" means a claim of an issued and unexpired patent that is in force included within the **Licensed Patent Rights** which has not been revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction (which decision is not appealable or has not been appealed within the time allowed for appeal), and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise.

3. GRANT OF RIGHTS

3.1 The **IC** hereby grants and the **Licensee** and its **Affiliates** accepts, subject to the terms and conditions of this **Agreement**, a nonexclusive license under, and to, the **Licensed Patent Rights** in the **Licensed Territory** to develop, make and have made, to develop and have developed, to register and have registered, to use and have used, to distribute and have distributed, to sell and have sold, to offer to sell, and to import and export any **Licensed Products** in the **Licensed Fields of Use** and to practice and have practiced any **Licensed Processes** in the **Licensed Fields of Use**. For clarity, LogicBio will pay royalties for **Licensed Products** that are no longer covered by the **Licensed Patent Rights** but enjoy **Orphan Drug Exclusivity** in a country (as defined in Paragraph 2.14 ("**Licensed Product**")).

3.2 This **Agreement** confers no license or rights by implication, estoppel, or otherwise under any patent applications or patents of the **IC** other than the **Licensed Patent Rights** regardless of whether these patents are dominant or subordinate to the **Licensed Patent Rights**.

4. SUBLICENSING

4.1 Upon written approval, which shall include prior review of any sublicense agreement by the **IC** and which shall not be unreasonably withheld, the **Licensee** may enter into sublicensing agreements under the **Licensed Patent Rights** and the **Orphan Drug Designation** only when it concurrently licenses proprietary or in-licensed intellectual property rights. For the avoidance of doubt, the **Licensee** does not have the right to solely sublicense the **Licensed Patent Rights or** the **Orphan Drug Designation**.

4.2 The **Licensee** agrees that any sublicenses granted by it shall provide that the obligations to the **IC** of Paragraphs 5.1, 5.2, 8.1, 10.1, 10.3, 12.5, and 13.7-13.9 of this **Agreement** shall be binding upon the **Sublicensee** as if it were a party to this **Agreement**. The **Licensee** further agrees to include copies of these Paragraphs in all sublicense agreements.

4.3 Any sublicenses granted by the **Licensee** shall provide for the termination of the sublicense, or the conversion to a license directly between the **Sublicensee** and the **IC**, at the option of the **Sublicensee**, upon termination of this **Agreement** under Article 13. This conversion is subject to the **IC** approval and contingent upon acceptance by the **Sublicensee** of the remaining provisions of this **Agreement**.

4.4 The **Licensee** agrees to forward to the **IC** a complete copy of each fully executed sublicense agreement postmarked within [***] ([***]) days of the execution of the agreement. To the extent permitted by law, the **IC** agrees to maintain each sublicense agreement in confidence.

5. STATUTORY AND NIH REQUIREMENTS AND RESERVED GOVERNMENT RIGHTS

5.1 Prior to the **First Commercial Sale**, and upon agreement of the parties, the **Licensee** shall provide the **IC** with reasonable quantities of **Licensed Products** or materials made through the **Licensed Processes** for the **IC's** research use. Such materials shall be considered the confidential information of the Licensee and will not be disclosed by the IC without the prior written consent of the Licensee.

5.2 The **Licensee** agrees that products used or sold in the United States embodying **Licensed Products** or produced through use of **Licensed Processes** shall be manufactured substantially in the United States, unless a written waiver is obtained in advance from the **IC**.

6. ROYALTIES AND REIMBURSEMENT

6.1 The **Licensee** agrees to pay the **IC** a noncreditable, nonrefundable license issue royalty as set forth in Appendix C.

6.2 The **Licensee** agrees to pay the **IC** a minimum annual royalty as set forth in Appendix C.

6.3 The **Licensee** agrees to pay the **IC** earned royalties as set forth in Appendix C.

6.4 The **Licensee** agrees to pay the **IC** benchmark royalties as set forth in Appendix C.

6.5 The **Licensee** agrees to pay the **IC** sublicensing royalties as set forth in Appendix C.

6.6 The **Licensee** agrees to pay the **IC** the assignment royalty as set forth in Paragraph 14.7.

6.7 A patent or patent application licensed under this **Agreement** shall cease to fall within the **Licensed Patent Rights** or **the Orphan Drug Exclusivity** for the purpose of computing earned royalty payments in any given country on the latest of the date(s) that:

(a) the application has been abandoned and not continued;

(b) the patent expires or irrevocably lapses; or

(c) the patent has been held to be invalid or unenforceable by an unappealed or unappealable decision of a court of competent jurisdiction or administrative agency;

and an **Orphan Drug Exclusivity** terminates or expires in a particular country or region.

6.8 No multiple royalties shall be payable because any **Licensed Products** or **Licensed Processes** are covered by more than one of the **Licensed Patent Rights**.

6.9 On sales of **Licensed Products** by the **Licensee** to **Sublicensees** or on sales made in other than an arms-length transaction, the value of the **Net Sales** attributed under this Article 6 to this transaction shall be that which would have been received in an arms-length transaction, based on sales of like quantity and quality products on or about the time of this transaction.

6.10 With regard to unreimbursed expenses associated with the preparation, filing, prosecution, and maintenance of all patent applications and patents included within the **Licensed Patent Rights** and paid by the **IC** on or after the **Effective Date** of this **Agreement**, the **IC**, at its sole option, may require the **Licensee**:

(a) to pay the **IC** on an annual basis, within [***] ([***]) days of the **IC's** submission of a statement and request for payment, a royalty amount equivalent to [***] percent ([***]%) of these unreimbursed expenses paid during the previous calendar year(s); *provided* that if **IC** grants one or more additional licenses to one or more **Third Parties**, then the **Licensee** shall pay the **IC** [***] percent ([***]%) of a pro-rated portion of such unreimbursed expenses calculated by dividing the total patent costs paid during the previous calendar year(s) by two (2) times the number of additional licenses of record.

6.11 The **IC** agrees, upon written request, to provide the **Licensee** with summaries of patent prosecution invoices for which the **IC** has requested payment from the **Licensee** under Paragraphs 6.9 and 6.10. The **Licensee** agrees that all information provided by the **IC** related to patent prosecution costs shall be treated as confidential commercial information and shall not be released to a **Third Party** except as required by law or a court of competent jurisdiction.

6.12 The **Licensee** may elect to surrender its rights in any country of the **Licensed Territory** under any of the **Licensed Patent Rights** upon [***] ([***]) days written notice to the **IC** and owe no payment obligation under Paragraph 6.10 for patent-related expenses paid in that country after the effective date of the written notice.

7. PATENT FILING, PROSECUTION, AND MAINTENANCE

7.1 The **IC** agrees to take responsibility for the preparation, filing, prosecution, and maintenance of any and all patent applications or patents included in the **Licensed Patent Rights**.

8. RECORD KEEPING

8.1 The **Licensee** agrees to keep accurate and correct records of **Licensed Products** made, used, sold, or imported and **Licensed Processes** practiced under this **Agreement** appropriate to determine the amount of royalties due the **IC**. These records shall be retained for at least five (5) years following a given reporting period and shall be available during normal business hours for inspection, at the expense of the **IC**, by an accountant or other designated auditor selected by the **IC** for the sole purpose of verifying reports and royalty payments hereunder. The accountant or auditor shall only disclose to the **IC** information relating to the accuracy of reports and royalty payments made under this **Agreement**. If an inspection shows an underreporting or underpayment in excess of [***]percent ([***]%) for any twelve (12) month period, then the **Licensee** shall reimburse the **IC** for the cost of the inspection at the time the **Licensee** pays the unreported royalties, including any additional royalties as required by Paragraph 9.7. All royalty payments required under this Paragraph shall be due within [***] ([***]) days of the date the **IC** provides the **Licensee** notice of the payment due.

9. REPORTS ON PROGRESS, BENCHMARKS, SALES, AND PAYMENTS

9.1 Prior to signing this **Agreement**, the **Licensee** has provided the **IC** with the **Commercial Development Plan** under which the **Licensee** intends to bring the subject matter of the **Licensed Patent Rights** to the point of **Practical Application**.

9.2 The **Licensee** shall report to the **IC** the dates for achieving **Benchmarks** specified in Appendix D and the **First Commercial Sale** in each country in the **Licensed Territory** within [***] ([***]) days of such occurrences.

9.3 The **Licensee** shall submit to the **IC**, within [***] ([***]) days after each calendar half-year ending June 30 and December 31, a royalty report, as described in the example in Appendix F, setting forth for the preceding half-year period the amount of the **Licensed Products** sold or **Licensed Processes** practiced by or on behalf of the **Licensee** in each country within the **Licensed Territory**, the **Net Sales**, and the amount of royalty accordingly due. With each royalty report, the **Licensee** shall submit payment of earned royalties due. If no earned royalties are due to the **IC** for any reporting period, the written report shall so state. The royalty report shall be certified as correct by an authorized officer of the **Licensee** and shall include a detailed listing of all deductions made under Paragraph 2.17 to determine **Net Sales** made under Article 6 to determine royalties due.

9.4 The **Licensee** agrees to forward semi-annually to the **IC** a copy of these reports received by the **Licensee** from its **Sublicensees** during the preceding half-year period as shall be pertinent to a royalty accounting to the **IC** by the **Licensee** for activities under the sublicense.

9.5 Royalties due under Article 6 shall be paid in U.S. dollars and payment options are listed in Appendix G. For conversion of foreign currency to U.S. dollars, the conversion rate shall be the New York foreign exchange rate quoted in *The Wall Street Journal* on the day that the payment is due, and any loss of exchange, value, taxes, or other expenses incurred in the transfer or conversion to U.S. dollars shall be paid entirely by the **Licensee**. The royalty report required by Paragraph 9.4 shall be mailed to the **IC** at its address for **Agreement** Notices indicated on the Signature Page.

9.6 The **Licensee** shall be solely responsible for determining if any tax on royalty income is owed outside the United States and shall pay this tax and be responsible for all filings with appropriate agencies of foreign governments.

9.7 Additional royalties may be assessed by the **IC** on any payment that is more than [***] ([***]) days overdue at the rate of [***] percent ([***]%) per month. This [***] percent ([***]%) per month rate may be applied retroactively from the original due date until the date of receipt by the **IC** of the overdue payment and additional royalties. The payment of any additional royalties shall not prevent the **IC** from exercising any other rights it may have as a consequence of the lateness of any payment.

9.8 All plans and reports required by this Article 9 and marked "confidential" by the **Licensee** shall, to the extent permitted by law, be treated by the **IC** as commercial and financial information obtained from a person and as privileged and confidential, and any proposed disclosure of these records by the **IC** under the Freedom of Information Act (FOIA), 5 U.S.C. §552 shall be subject to the predisclosure notification requirements of 45 CFR §5.65(d).

10. PERFORMANCE

10.1 The **Licensee** shall use its reasonable commercial efforts to bring the **Licensed Products** and **Licensed Processes** to **Practical Application**. "Reasonable commercial efforts" for the purposes of this provision shall include commercially reasonable efforts to adhere to the **Commercial Development Plan** in Appendix E and performance of the **Benchmarks** in Appendix D. The efforts of a Sublicensee shall be considered the efforts of the **Licensee**.

10.2 Upon the **First Commercial Sale**, until the expiration or termination of this **Agreement**, the Licensee shall use its reasonable commercial efforts to make **Licensed Products** and **Licensed Processes** reasonably available in the United States.

10.3 The **Licensee** agrees that, to the extent commercially reasonable, after its **First Commercial Sale,** to make reasonable quantities of **Licensed Products** or materials produced through the use of **Licensed Processes** available to patient assistance programs.

10.4 The **Licensee** agrees, after its **First Commercial Sale** and as part of its marketing and product promotion, to develop educational materials (e.g., brochures, website, etc.) directed to patients and physicians detailing the **Licensed Products** or medical aspects of the prophylactic and therapeutic uses of the **Licensed Products**.

10.5 The **Licensee** agrees to supply, to the Mailing Address for **Agreement** Notices indicated on the Signature Page, the Office of Technology Transfer, **NIH** with inert samples of the **Licensed Products** or **Licensed Processes** or their packaging for educational and display purposes only.

11. INFRINGEMENT AND PATENT ENFORCEMENT

11.1 The **IC** and the **Licensee** agree to notify each other promptly of each infringement or possible infringement of the **Licensed Patent Rights**, as well as, any facts which may affect the validity, scope, or enforceability of the **Licensed Patent Rights** of which either Party becomes aware.

11.2 In the event that a declaratory judgment action alleging invalidity of any of the **Licensed Patent Rights** shall be brought against the **IC**, the **IC** agrees to notify the **Licensee** that an action alleging invalidity has been brought. The **IC** does not represent that it shall commence legal action to defend against a declaratory action alleging invalidity. The **Licensee** shall take no action to compel the **Government** either to initiate or to join in any declaratory judgment action. Should the **Government** be made a party to any suit by motion or any other action of the **Licensee**, the **Licensee** shall reimburse the **Government** for any costs, expenses, or fees, which the **Government** incurs as a result of the motion or other action. Upon the **Licensee's** payment of all costs incurred by the **Government** as a result of the **Licensee's** joinder motion or other action, these actions by the **Licensee** shall not be considered a default in the performance of any material obligation under this **Agreement**.

12. NEGATION OF WARRANTIES AND INDEMNIFICATION

12.1 The **IC** offers no warranties other than those specified in Article 1.

12.2 The **IC** does not warrant the validity of the **Licensed Patent Rights** and makes no representations whatsoever with regard to the scope of the **Licensed Patent Rights**, or that the **Licensed Patent Rights** may be exploited without infringing other patents or other intellectual property rights of **Third Parties**.

12.3 THE **IC** MAKES NO WARRANTIES, EXPRESSED OR IMPLIED, OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF ANY SUBJECT MATTER DEFINED BY THE CLAIMS OF THE **LICENSED PATENT RIGHTS** OR TANGIBLE MATERIALS RELATED THERETO.

12.4 The **IC** does not represent that it shall commence legal actions against **Third Parties** infringing the **Licensed Patent Rights**.

12.5 The **Licensee** shall indemnify and hold the **IC**, its employees, students, fellows, agents, and consultants harmless from and against all liability, demands, damages, expenses, and losses, including but not limited to death, personal injury, illness, or property damage in connection with or arising out of:

(a) the use by or on behalf of the **Licensee**, its **Sublicensees**, its **Affiliates**, or their respective directors, employees, or **Third Parties** (on behalf of the **Licensees**, its **Sublicensees**, or **Affiliates**) of any **Licensed Patent Rights**; or

(b) the design, manufacture, distribution, or use of any **Licensed Products**, **Licensed Processes** or materials, by the **Licensee**, or other products or processes developed in connection with or arising out of the **Licensed Patent Rights**.

12.6 The **Licensee** agrees to maintain a liability insurance program consistent with sound business practice.

13. TERM, TERMINATION, AND MODIFICATION OF RIGHTS

13.1 This Agreement is effective when signed by all parties, (the "Effective Date"), and shall extend to the expiration of the last to expire of (a) the Licensed Patent Rights and (b) the U.S. Orphan Drug Exclusivity, European Orphan Drug Exclusivity, Australian Orphan Drug Exclusivity, Japanese Orphan Drug Exclusivity or equivalent foreign Orphan Drug Exclusivity with respect to any Licensed Product, unless sooner terminated under Article 6 or 13.

13.2 In the event that the **Licensee** is in default in the performance of any material obligations under this **Agreement**, including but not limited to the obligations listed in Paragraph 13.5, and if the default has not been remedied within [***] ([***]) days after the date of notice in writing of the default, the **IC** may terminate this **Agreement** by written notice and pursue outstanding royalties owed through procedures provided by the Federal Debt Collection Act.

13.3 In the event that the **Licensee** becomes insolvent, files a petition in bankruptcy, has such a petition filed against it, determines to file a petition in bankruptcy, or receives notice of a **Third Party's** intention to file an involuntary petition in bankruptcy, the **Licensee** shall immediately notify the **IC** in writing.

13.4 The **Licensee** shall have a unilateral right to terminate this **Agreement** in any country or territory by giving the **IC** sixty (60) days written notice to that effect.

13.5 The **IC** shall specifically have the right to terminate or modify, at its option, this **Agreement**, if the **IC** determines that the **Licensee**:

(a) has willfully made a false statement of, or willfully omitted, a material fact in the license application or in any report required by this **Agreement**;

(b) has committed a material breach of a covenant or agreement contained in this **Agreement**;

(c) is not keeping **Licensed Products** or **Licensed Processes** reasonably available to the public after **First Commercial Sale**;

(d) cannot reasonably satisfy unmet health and safety needs; or

(e) cannot reasonably justify a failure to comply with the domestic production requirement of Paragraph 5.2, unless waived.

13.6 In making the determination referenced in Paragraph 13.5, the **IC** shall take into account the normal course of such commercial development programs conducted with sound and reasonable business practices and judgment and the annual reports submitted by the **Licensee** under Paragraph 9.2. Prior to invoking termination or modification of this **Agreement** under Paragraph 13.5, the **IC** shall give written notice to the **Licensee** providing the **Licensee** specific notice of, and a [***] ([***]) day opportunity to respond to, the **IC's** concerns as to the items referenced in 13.5(a)-13.5(g). If the **Licensee** fails to alleviate the **IC's** concerns as to the items referenced in 13.5(a)-13.5(g) or fails to initiate corrective action to the **IC's** satisfaction, the **IC** may terminate this **Agreement**.

13.7 The **IC** reserves the right according to 35 U.S.C. §209(d)(3) to terminate or modify this **Agreement** if it is determined that the action is necessary to meet the requirements for public use specified by federal regulations issued after the date of the license and these requirements are not reasonably satisfied by the **Licensee**.

13.8 Within [***] ([***]) days of receipt of written notice of the **IC's** unilateral decision to modify or terminate this **Agreement**, the **Licensee** may, consistent with the provisions of 37 CFR §404.11, appeal the decision by written submission to the designated the **IC** official. The decision of the designated **IC** official shall be the final agency decision. The **Licensee** may thereafter exercise any and all administrative or judicial remedies that may be available.

13.9 Within [***] ([***]) days of expiration or termination of this **Agreement** under this Article 13, a final report shall be submitted by the **Licensee**. Any royalty payments, including those incurred but not yet paid (such as the full minimum annual royalty), and those related to patent expense, due to the **IC** shall become immediately due and payable upon termination or expiration. If terminated under this Article 13, **Sublicensees** may elect to convert their sublicenses to direct licenses with the **IC** pursuant to Paragraph 4.3. Unless otherwise specifically provided for under this **Agreement**, upon termination or expiration of this **Agreement**, the **Licensee** shall return all **Licensed Products** or other materials included within the **Licensed Patent Rights** to the **IC** or provide the **IC** with written certification of the destruction thereof. The **Licensee** may not be granted additional the **IC** licenses if the final reporting requirement is not fulfilled.

14. GENERAL PROVISIONS

14.1 Neither party may waive or release any of its rights or interests in this **Agreement** except in writing. The failure of the **Government** to assert a right hereunder or to insist upon compliance with any term or condition of this **Agreement** shall not constitute a waiver of that right by the **Government** or excuse a similar subsequent failure to perform any of these terms or conditions by the **Licensee**.

14.2 This **Agreement** constitutes the entire agreement between the Parties relating to the subject matter of the **Licensed Patent Rights**, **Licensed Products** and **Licensed Processes**, and all prior negotiations, representations, agreements, and understandings are merged into, extinguished by, and completely expressed by this **Agreement**.

14.3 The provisions of this **Agreement** are severable, and in the event that any provision of this **Agreement** shall be determined to be invalid or unenforceable under any controlling body of law, this determination shall not in any way affect the validity or enforceability of the remaining provisions of this **Agreement**.

14.4 If either party desires a modification to this **Agreement**, the parties shall, upon reasonable notice of the proposed modification by the party desiring the change, confer in good faith to determine the desirability of the modification. No modification shall be effective until a written amendment is signed by the signatories to this **Agreement** or their designees.

14.5 The construction, validity, performance, and effect of this **Agreement** shall be governed by Federal law as applied by the Federal courts in the District of Columbia.

14.6 All **Agreement** notices required or permitted by this **Agreement** shall be given by prepaid, first class, registered or certified mail or by an express/overnight delivery service provided by a commercial carrier, properly addressed to the other party at the address designated on the Signature Page, or to any other address as may be designated in writing by such other party. **Agreement** notices shall be considered timely if such notices are received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Parties should request a legibly dated U.S. Postal Service postmark or obtain a dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailing.

14.7 This **Agreement** shall not be assigned or otherwise transferred (including any transfer by legal process or by operation of law, and any transfer in bankruptcy or insolvency, or in any other compulsory procedure or order of court) except to a purchaser of all or substantially of the **Licensee's** assets or to the **Licensee's Affiliate(s)** without the prior written consent of the **IC**. The parties agree that the identity of the parties is material to the formation of this **Agreement** and that the obligations under this **Agreement** are nondelegable. In the event that the **IC** approves a proposed assignment, the **Licensee** shall pay the **IC**, as an additional royalty, [***] percent ([***]%) of the fair market value of any consideration received for any assignment of this **Agreement** within [***] ([***]) days of the assignment.

14.8 The **Licensee** agrees in its use of any **IC**-supplied materials to comply with all applicable statutes, regulations, and guidelines, including the **NIH** and the **HHS** regulations and guidelines. The **Licensee** agrees not to use the materials for research involving human subjects or clinical trials in the United States without complying with 21 CFR Part 50 and 45 CFR Part 46. The **Licensee** agrees not to use the materials for research involving human subjects or clinical trials outside of the United States without notifying the **IC**, in writing, of the research or trials and complying with the applicable regulations of the appropriate national control authorities. Written notification to the **IC** of research involving human subjects or clinical trials outside of the United States shall be given no later than [***] ([***]) days prior to commencement of the research or trials.

14.9 The **Licensee** acknowledges that it is subject to and agrees to abide by the United States laws and regulations (including the Export Administration Act of 1979 and Arms Export Control Act) controlling the export of technical data, computer software, laboratory prototypes, biological materials, and other commodities. The transfer of these items may require a license from the appropriate agency of the **Government** or written assurances by the **Licensee** that it shall not export these items to certain foreign countries without prior approval of the agency. The **IC** neither represents that a license is or is not required or that, if required, it shall be issued.

14.10 The **Licensee** agrees to mark the **Licensed Products** or their packaging sold in the United States with all applicable U.S. patent numbers and similarly to indicate "Patent Pending" status. All **Licensed Products** manufactured in, shipped to, or sold in other countries shall be marked in a manner to preserve the **IC** patent rights in those countries.

14.11 By entering into this **Agreement**, the **IC** does not directly or indirectly endorse any product or service provided, or to be provided, by the **Licensee** whether directly or indirectly related to this **Agreement**. The **Licensee** shall not state or imply that this **Agreement** is an endorsement by the **Government**, the **IC**, any other **Government** organizational unit, or any **Government** employee. Additionally, the **Licensee** shall not use the names of the **IC**, **NIH**, **FDA** or **HHS** or the **Government** or their employees in any advertising, promotional, or sales literature without the prior written approval of the **IC**.

14.12 The Parties agree to attempt to settle amicably any controversy or claim arising under this **Agreement** or a breach of this **Agreement**, except for appeals of modifications or termination decisions provided for in Article 13. The **Licensee** agrees first to appeal any unsettled claims or controversies to the designated the **IC** official, or designee, whose decision shall be considered the final agency decision. Thereafter, the **Licensee** may exercise any administrative or judicial remedies that may be available.

14.13 Nothing relating to the grant of a license, nor the grant itself, shall be construed to confer upon any person any immunity from or defenses under the antitrust laws or from a charge of patent misuse, and the acquisition and use of rights pursuant to 37 CFR Part 404 shall not be immunized from the operation of state or Federal law by reason of the source of the grant.

14.14 Paragraphs 8.1, 9.7, 9.8, 12.1-12.5, 13.8, 13.9, 14.12 and 14.14 of this **Agreement** shall survive termination of this **Agreement**.

14.15 The terms and conditions of this **Agreement** shall, at the **IC's** reasonable discretion, be considered by the **IC** to be withdrawn from the **Licensee's** consideration and the terms and conditions of this **Agreement**, and the **Agreement** itself to be null and void, unless this **Agreement** is executed by the **Licensee** and a fully executed original is received by the **IC** within [***] ([***]) days from the date of the **IC** signature found at the Signature Page.

SIGNATURES BEGIN ON NEXT PAGE

NIH PATENT LICENSE AGREEMENT NONEXCLUSIVE – SUBLICENSABLE

SIGNATURE PAGE

For the **IC**:

[***] December 14, 2018
[***] Date

Director, Technology Transfer Office (TTO)
National Human Genome Research Institute (**NHGRI**)
National Institutes of Health Mailing Address or E-mail Address for **Agreement** notices and reports:

Mailing Address or E-mail Address for **Agreement** notices and reports:

License Compliance and Administration
Monitoring & Enforcement
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852-3804 U.S.A.

E-mail: LicenseNotices_Reports@mail.nih.gov

For the **Licensee** (Upon, information and belief, the undersigned expressly certifies or affirms that the contents of any statements of the **Licensee** made or referred to in this document are truthful and accurate.):

by:

/s/ Frederic Chereau
Signature of Authorized Official Date

Date 12/10/2018

Fred Chereau
Printed Name

Chief Executive Officer
Title

I. Official and Mailing Address for **Agreement** notices:

Thomas Wilton
Name

Chief Business Officer
Title

Mailing Address

[***] Portions of this exhibit have been redacted pursuant to a Confidential Treatment Request. An unredacted version of this exhibit has been filed separately with the Commission.

LogicBio, 610 Main Street, 3rd Floor, Cambridge, MA 02139

Email Address: twilton@logicbio.com

Phone: 215 316 9239

Fax:

II. Official and Mailing Address for Financial notices (the **Licensee's** contact person for royalty payments)

Mathias Jaffe
Name

Chief Financial Officer
Title

Mailing Address:

LogicBio, 610 Main Street, 3rd Floor, Cambridge, MA 02139

Email Address: mjaffe@logicbio.com

Phone: 617 959 7425

Fax:

Any false or misleading statements made, presented, or submitted to the **Government**, including any relevant omissions, under this **Agreement** and during the course of negotiation of this **Agreement** are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. §§3801-3812 (civil liability) and 18 U.S.C. §1001 (criminal liability including fine(s) and/or imprisonment).

APPENDIX A – PATENT(S) OR PATENT APPLICATION(S)

Patent(s) or Patent Application(s):

I. US Provisional Patent Application No.: 61/792,081
HHS Ref. No.: E-243-2012/0-US-01
Filing Date: March 15, 2013
Current Status: Expired

II. PCT Patent Application No.: PCT/2014/028045
HHS Ref. No.: E-243-2012/0-PCT-02
Filing Date: March 14, 2014
Current Status: Nationalized

III. EP Patent Application 14729502.6
HHS Ref. No.: E-243-2012/0-EP-03
Filing Date: March 14, 2014
Current Status: Issued 2968602

IV. US Patent Application No.: 14/773,885
HHS Ref. No.: E-243-2012/0-US-04
Filing Date: September 09, 2015
Current Status: Issued US 9,719,080

V. US Patent Application No.: 15/070,787 (Continuation in Part)
HHS Ref. No.: E-243-2012/1-US-01
Filing Date: March 15, 2016
Current Status: Issued US 9,944,918

VI. US Patent Application No.: 15/633,964 (CON)
HHS Ref. No.: E-243-2012/0-US-05
Filing Date: June 27, 2017
Current Status: Pending

VII. BE Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-BE-06
Filing Date: March 14, 2014
Current Status: Issued

VIII. CH Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-CH-07
Filing Date: March 14, 2014
Current Status: Issued

IX. DE Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-DE-08
Filing Date: March 14, 2014
Current Status: Issued

X. DK Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-DK-09
Filing Date: March 14, 2014
Current Status: Issued

XI. ES Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-ES-10
Filing Date: March 14, 2014
Current Status: Issued

XII. FR Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-FR-11
Filing Date: March 14, 2014
Current Status: Issued

XIII. GB Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-GB-12
Filing Date: March 14, 2014
Current Status: Issued

XIV. IE Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-IE-13
Filing Date: March 14, 2014
Current Status: Issued

XV. IT Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-IT-14
Filing Date: March 14, 2014
Current Status: Issued

XVI. LU Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-LU-15
Filing Date: March 14, 2014
Current Status: Issued

XVII. NL Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-NL-16
Filing Date: March 14, 2014
Current Status: Issued

XVIII. SE Patent Application No.: 14729502.6
HHS Ref. No.: E-243-2012/0-SE-17
Filing Date: March 14, 2014
Current Status: Issued

[***] Portions of this exhibit have been redacted pursuant to a Confidential Treatment Request. An unredacted version of this exhibit has been filed separately with the Commission.

APPENDIX B – LICENSED FIELDS OF USE AND TERRITORY

I. **Licensed Fields of Use:**

(a) Research, development, manufacture and commercialization of pharmaceutical products for the treatment and/or prevention of Methylmalonic Acidemia (MMA) using gene therapy constructs in humans that incorporate the Licensed Product(s).

II. **Licensed Territory: Worldwide**

APPENDIX C – ROYALTIES

Royalties:

The **Licensee** agrees to pay to the **IC** a noncreditable, nonrefundable license issue royalty in the amount of Twenty Five Thousand Dollars ($25,000.00) within [***] ([***]) days from the **Effective Date** of this **Agreement.**

The **Licensee** agrees to pay to the **IC** a nonrefundable minimum annual royalty in the amount of [***] Dollars ($[***]) as follows:

The minimum annual royalty payments are due and payable on January 1 of each calendar year and may be credited against any earned royalties due for sales made in that year.

Sublicensing Royalties:

The **Licensee** agrees to pay the **IC** additional sublicensing royalties of:

[***] percent ([***]%) of any upfront payment in cash or of the fair market value of any upfront non-cash consideration received by the **Licensee** for granting each sublicense, within [***] ([***]) days of the execution of each sublicense.

Running Royalties on Net Sales:

The **Licensee** agrees to pay the **IC** earned royalties of [***] percent ([***]%) on U.S. based **Net Sales** by or on behalf of the **Licensee**, on a Licensed Product-by-Licensed Product basis, until the last to expire of the **Licensed Patent Rights** or the **U.S. Orphan Drug Exclusivity** for a Licensed Product.

The **Licensee** agrees to pay the **IC** earned royalties of [***] percent ([***]%) on European **Net Sales** by or on behalf of the **Licensee**, on a Licensed Product-by-Licensed Product basis, until the last to expire of the **Licensed Patent Rights** or **European Orphan Drug Exclusivity** for a Licensed Product.

The **Licensee** agrees to pay the **IC** earned royalties of [***] percent ([***]%) on "rest of the world" (ROW) country/ies (i.e., other than the US or Europe) based **Net Sales** by or on behalf of the **Licensee**, on a Licensed Product-by-Licensed Product basis, until the last to expire of the **Licensed Patent Rights** or the **Orphan Drug Exclusivity** for a Licensed Product in the corresponding ROW countries (if applicable).

For clarity, Licensee shall not pay running royalties on Net Sales of a Licensed Product in any country where (a) the development, manufacture, use, distribution, sale or importation of the Licensed Product are no longer within the scope of one or more claims of the Licensed Patents Rights in the country that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction, and (b) such Licensed Product does not have valid Orphan Drug Exclusivity.

Benchmark Royalties:

The **Licensee** agrees to pay the **IC Benchmark** royalties within [***] ([***]) days of achieving each **Benchmark**:

(a) [***] dollars ($[***]) for initiation of the **Licensee**-sponsored **Phase 1 Clinical Study (trial)** or foreign equivalent in the **Licensed Field of Use**.

(b) [***] dollars ($[***]) for initiation of the **Licensee**-sponsored **Phase 2 Clinical Study (trial)** or foreign equivalent in the **Licensed Field of Use** or, in the case of the absence of **Phase 2 Clinical Study (trial)** for an **Orphan Indication**, **a pivotal trial**.

(c) [***] dollars ($[***]) for initiation of the first **Licensee**-sponsored **Phase 3 Clinical Study (trial)** or foreign equivalent in the **Licensed Field of Use** or, in the case of the absence of **Phase 3 Clinical Study (trial)** for an **Orphan Indication, a pivotal trial.**

(d) [***] dollars ($[***]) for submission of the first new drug application (NDA) or foreign equivalent as defined by the **FDA** for a **Licensed Product** or **Licensed Process** for an **Orphan Indication** or in the **Licensed Field of Use**.

(e) [***] dollars ($[***]) for submission of the first new drug application (or European equivalent thereof) for EMA approval for a **Licensed Product** or **Licensed Process** for an **Orphan Indication** or in the **Licensed Field of Use**.

(f) [***] dollars ($[***]) for submission of the first new drug application (or Japanese equivalent thereof) for Japanese regulatory approval for a **Licensed Product** or **Licensed Process** for an **Orphan Indication** or in the **Licensed Field of Use**.

(g) [***] dollars ($[***]) upon the **First Commercial Sale** in the **Licensed Field of Use** for **MMA**, in the United States.

(h) [***] Dollars ($[***]) upon the **First Commercial Sale** in the **Licensed Field of Use** for **MMA**, in Europe.

(i) [***] Dollars ($[***]) upon the **First Commercial Sale** in the **Licensed Field of Use** for **MMA**, outside the US or Europe.

Initiation of a clinical trial study is defined as the first patient dosed in said clinical trial study.

The first time the Cumulative **Net Sales** of all **Licensed Products** achieve the following thresholds, the **Licensee** pays the following one-time **Benchmark** royalties:

a) [***] dollars ($[***]) when the cumulative **Net Sales** of all **Licensed Products** reaches [***] dollars ($[***]).

b) [***] dollars ($[***]) when the cumulative **Net Sales** of all **Licensed Products** reaches [***] dollars ($[***]).

c) [***] dollars ($[***]) when the cumulative **Net Sales** of all **Licensed Products** reaches [***] dollars ($[***]).

d) [***] dollars ($[***]) when the cumulative **Net Sales** of all **Licensed Products** reaches [***] dollars ($[***]).

e) [***] dollars ($[***]) when the cumulative **Net Sales** of all **Licensed Products** reaches [***] dollars ($[***]).

Priority Review Voucher Royalties:

If a Priority Review Voucher or a foreign equivalent is granted to the **Licensee** by the FDA or another regulatory agency (such as but not limited to the Australian TGA, the EMA or the Japanese Pharmaceuticals and Medical Devices Agency (PMDA)) for a Licensed Product, the Licensee agrees to make one of the following Benchmark royalty payments for each Priority Review Voucher or foreign equivalent:

(1) [***] percent ([***]%) of the transfer or sale price paid or fair market value of any non-cash consideration by the Third Party to the **Licensee** or **Affiliate** for the sold or transferred **Priority Review Voucher** or a foreign equivalent shall be due and payable to the IC within [***] ([***]) days following **Licensee's** receipt of funds from such third-party sale or transfer; or

(2) If the **Licensee** or **Affiliate** is granted **Priority Review** or a foreign equivalent of **Licensee's BLA, NDA, ANDA** or other regulatory application by the **FDA** for a product under the **Priority Review Voucher** or a foreign equivalent, and the **Licensee** or **Affiliate** uses the Voucher to obtain approval of its own or its Affiliate's therapeutic for an **Orphan Indication** or in the Licensed Field of Use, [***] percent ([***]%) of the fair market value shall be due and payable to the **IC** within [***] days ([***]) following the grant of the **Priority Review** by the **FDA** or its foreign equivalent.

*For the sake of clarity, **Licensee** shall have no further obligation to pay **Benchmark Royalties** after the expiration or termination of this Agreement, and on a per-country basis or per-region basis (e.g., European Union), **Net Sales** in a particular country or region where there is no valid **Licensed Patent Rights** or **Orphan Drug Exclusivity** shall not contribute to the cumulative **Net Sales** for purposes of calculating **Benchmark Royalties**.*

APPENDIX D – BENCHMARKS

1. [***]
2. [***]
3. [***]

APPENDIX E – COMMERCIAL DEVELOPMENT PLAN

LB-001 is our lead GeneRide product candidate, which we are developing for the treatment of MMA in patients with the MUT mutation.

LB-001 consists of a DNA construct including a gene encoding the human *MUT* enzyme encapsulated in an AAV capsid. The *MUT* enzyme coding sequence is coupled to the 2A peptide sequence and surrounded by homology guides that drive the integration of the *MUT* gene and the 2A peptide sequence into the chromosomal locus for the albumin gene. Based on the way our construct integrates into the albumin locus, the *MUT* gene is then expressed resulting in synthesis of *MUT* enzyme as a separate protein from albumin. We chose LK03, the AAV capsid we use in LB-001, because it has been optimized to target human liver cells.

In collaboration with our partners at NHI, LogicBio has demonstrated the safety and efficacy of LB-001 in mouse models of MMA, and is planning to submit an IND for the LB-001 program by the end of 2019. We recently completed a $80M IPO which has provided sufficient funds to progress the LB-001 program to a first in human study in 2020. Assuming successful completion of this study LogicBio will progress the program to pivotal studies.

APPENDIX F – EXAMPLE ROYALTY REPORT

Required royalty report information includes:

- License reference number (L-XXX-200X/0)
- Reporting period
- Catalog number and units sold of each Licensed Product (domestic and foreign)
- Gross Sales per catalog number per country
- Total Gross Sales
- Itemized deductions from Gross Sales
- Total Net Sales
- Earned Royalty Rate and associated calculations
- Gross Earned Royalty
- Adjustments for Minimum Annual Royalty (MAR) and other creditable payments made
- Net Earned Royalty due

Example

Catalog Number	Product Name	Country	Units Sold	Gross Sales (US$)
1	A	US	250	62,500
1	A	UK	32	16,500
1	A	France	25	15,625
2	B	US	0	0
3	C	US	57	57,125
4	D	US	12	1,500
			Total Gross Sales	153,250
			Less Deductions:	
			Freight	3,000
			Returns	7,000
			Total Net Sales	143,250
			Royalty Rate	8%
			Royalty Due	11,460
			Less Creditable Payments	10,000
			Net Royalty Due	**1,460**

APPENDIX G – ROYALTY PAYMENT OPTIONS

[***]

Exhibit 21.1

Subsidiaries of the Registrant

Name	Ownership Percentage	Jurisdiction of Organization
LOGICBIO THERAPEUTICS RESEARCH LTD	100%	Israel
LOGICBIO AUSTRALIA PTY LIMITED	100%	Australia
LOGICBIO SECURITIES CORPORATION	100%	Delaware

Exhibit 31.1

CERTIFICATIONS

I, Frederic Chereau, certify that:

1. I have reviewed this Annual Report on Form 10-K of LogicBio Therapeutics, 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 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 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: April 1, 2019

By: /s/ Frederic Chereau
Frederic Chereau
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Matthias Jaffé, certify that:

1. I have reviewed this Annual Report on Form 10-K of LogicBio Therapeutics, 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 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 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: April 1, 2019

By: /s/ Matthias Jaffé
Matthias Jaffé
Chief Financial Officer
(Principal 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 the Annual Report on Form 10-K of LogicBio Therapeutics, Inc. (the "Company") for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to the best of his knowledge:

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

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

Date: April 1, 2019

By: /s/ Frederic Chereau
Frederic Chereau
President and Chief Executive Officer
(Principal Executive Officer)

Date: April 1, 2019

By: /s/ Matthias Jaffé
Matthias Jaffé
Chief Financial Officer
(Principal Financial Officer)