As confidentially submitted to the Securities and Exchange Commission on April 16, 2021. This draft registration statement has not been filed publicly with the Securities and Exchange Commission and all information contained herein remains confidential.

Registration No. 333-

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

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

GRAPHITE BIO, INC.
(Exact name of Registrant as specified in its charter)

Delaware	**2836**	**84-4867570**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

279 East Grand Avenue, Suite 430
South San Francisco, CA 94080
(650) 484-0886
(Address, including zip code and telephone number, including area code, of Registrant's principal executive offices)

Josh Lehrer, M.D.
Chief Executive Officer
279 East Grand Avenue, Suite 430
South San Francisco, CA 94080
(650) 484-0886
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Mitchell S. Bloom **Maggie Wong** **Anitha Anne** **Goodwin Procter LLP** **Three Embarcadero Center, Floor 28** **San Francisco, CA 94111** **(415) 733-6000**	**Josh Lehrer, M.D.** **Chief Executive Officer** **279 East Grand Avenue, Suite 430** **South San Francisco, CA 94080** **(650) 484-0886**	**Charles S. Kim** **Kristin VanderPas** **Dave Peinsipp** **Denny Won** **Cooley LLP** **4401 Eastgate Mall** **San Diego, CA 92121** **(858) 550-6000**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

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.

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 7(a)(2)(B) of the Securities Act. ☐

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Aggregate Offering Price(1)**	**Amount of Registration Fee(2)**
Common Stock, par value $0.00001 per share	$	$

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act. Includes the offering price of any additional shares that the underwriters have the option to purchase, solely to cover over-allotments.

(2) Calculated pursuant to Rule 457(o) under the Securities Act based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED , 2021.

Shares

Common Stock

This is an initial public offering of shares of common stock by Graphite Bio, Inc.

We are offering shares of our common stock. Prior to this offering, there has been no public market for our common stock. It is currently estimated that the initial public offering price per share will be between $ and $. We intend to apply to list our common stock on the Nasdaq Global Market under the symbol "GRPH."

We are an emerging growth company under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. See the section titled "Risk Factors" beginning on page 15.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) See the section titled "Underwriting" for additional disclosure regarding the estimated underwriting discounts and commissions and estimated offering expenses.

We have granted the underwriters the right to purchase up to an additional shares of common stock solely to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment in New York, New York on , 2021.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

Morgan Stanley **BofA Securities** **Cowen** **SVB Leerink**

, 2021

TABLE OF CONTENTS

We and the underwriters have not authorized anyone to provide you with any information other than that contained in this prospectus, any amendment or supplement to this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making an offer to sell, and seeking offers to buy, these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

Through and including , 2021 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described in the sections titled "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," and "Business." Unless otherwise stated, all references to "us," "our," "Graphite," "we," the "Company" and similar designations refer to Graphite Bio, Inc.

Overview

We are a clinical-stage, next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to potentially cure a wide range of serious and life-threatening diseases. We are pioneering a precision gene editing approach to achieve one of medicine's most elusive goals: to precisely "find & replace" any gene in the genome. Our next-generation gene editing platform allows us to precisely correct mutations, replace entire disease-causing genes with normal genes, or insert new genes into predetermined, safe locations. We believe our approach could enable nearly limitless applications to transform human health, including directly correcting mutations, engineering cells to permanently deliver therapeutic proteins, and precisely engineering effector cells to treat or cure a wide range of serious genetic and other diseases, including cancer, autoimmune and neurodegenerative diseases.

Our lead product candidate GPH101 is a highly differentiated approach with the potential to directly correct the mutation that causes sickle cell disease (SCD) and restore normal adult hemoglobin (HgbA) expression. Curing sickle cell disease by correcting the disease-causing point mutation to normal is viewed as the gold-standard for curing SCD and has been the dream of treating physicians for generations. We have received clearance of our Investigational New Drug (IND) and we intend to enroll the first patient in a Phase 1/2 clinical trial of GPH101 in . We are also advancing our research programs and pipeline of potentially one-time curative therapies for a wide range of genetic and other serious diseases and intend to file an IND for a second program by .

Our technology builds on first-generation proven CRISPR technology to achieve high rates of targeted gene integration. Our technology was developed in the Stanford laboratories of our two scientific founders, both pioneers in gene therapy and gene editing: Matthew Porteus, M.D., Ph.D., and Maria Grazia Roncarolo, M.D. Dr. Porteus is considered to be one of the founders of the field of gene editing and was a scientific founder of CRISPR Therapeutics. He was the first to demonstrate that an engineered nuclease could be used to correct genes by harnessing precision cellular DNA repair machinery. Dr. Roncarolo is a pioneer in multipotent hematopoietic stem cell (HSC) gene therapy and her work led to the first approved HSC gene therapy product. She established and is Director of the Stanford Center for Definitive and Curative Medicine to treat patients with currently incurable diseases through the development of innovative stem cell- and gene-based therapies. Drs. Porteus and Roncarolo, both practicing physicians, came together with the conviction that targeted gene integration could lead to an entirely new class of potentially curative therapies.

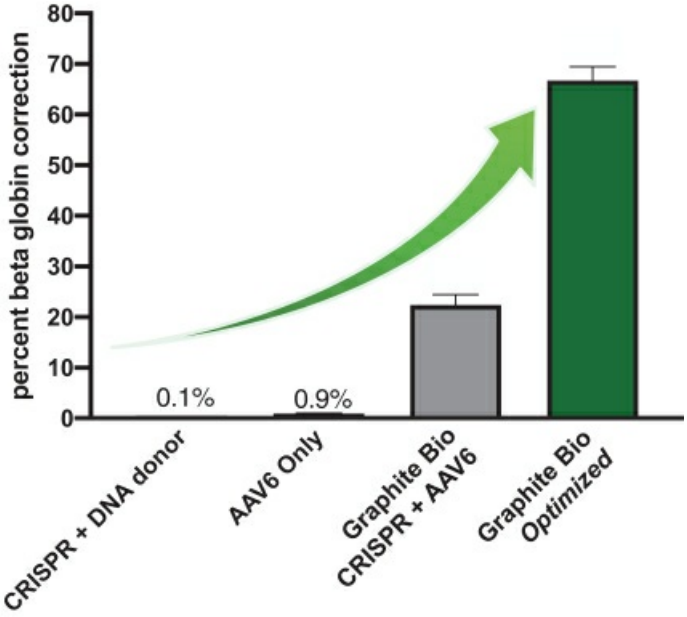
Our approach has broad therapeutic applications and has enabled high efficiency targeted gene integration in a wide range of primary human cell types. In our initial programs, we apply our approach *ex vivo* in a patient's own HSCs, which are reinfused after gene integration (autologous HSCT). HSCs are multipotent stem and progenitor cells that can give rise to all cells of the blood and immune system and have proven their curative potential across dozens of diseases as demonstrated by allogenic HSC transplant (allo-HSCT).

Our approach can be thought of as "find & replace," using CRISPR to find a target gene and homology directed repair (HDR) to replace DNA in the target gene with DNA copied from a template. We create a precise

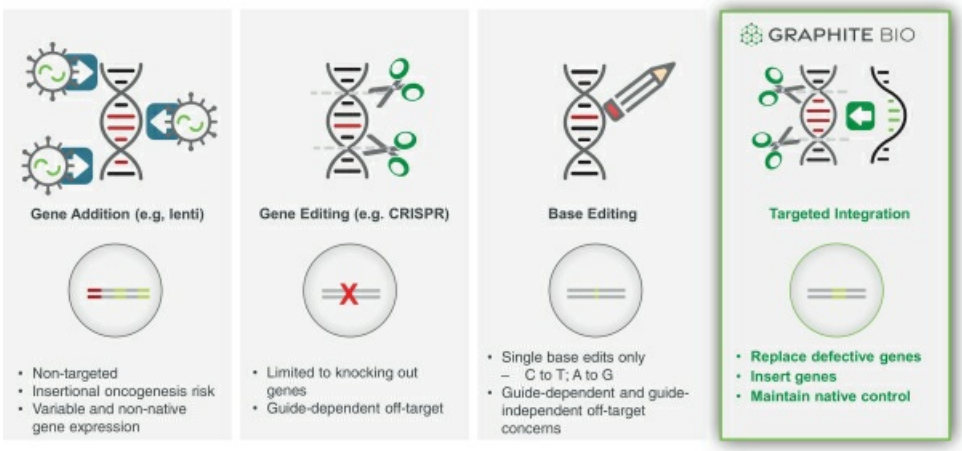
incision in a target gene using a modified, high fidelity CRISPR-based nuclease and then induce conditions in target cells that overwhelmingly favor HDR, a natural and precise cellular DNA repair process. Using a non-integrating AAV6 vector, we deliver a donor DNA template strand to the target gene which is copied via HDR to create a new coding strand. We then apply our HSC biology expertise to optimally engineer and manufacture HSCs, a historically intractable cell type for harnessing HDR. Using our next-generation gene editing approach, we have achieved gene integration efficiencies in excess of curative thresholds and demonstrated preclinical proof-of-concept across multiple diseases models. Beyond GPH101, our pipeline includes multiple programs including GPH201 for XSCID, our first gene replacement program, and GPH301 for Gaucher disease, our first targeted gene insertion program, and multiple undisclosed programs in both HSCs and other cell types.

Our approach differs from first generation gene and base editing technologies due to:

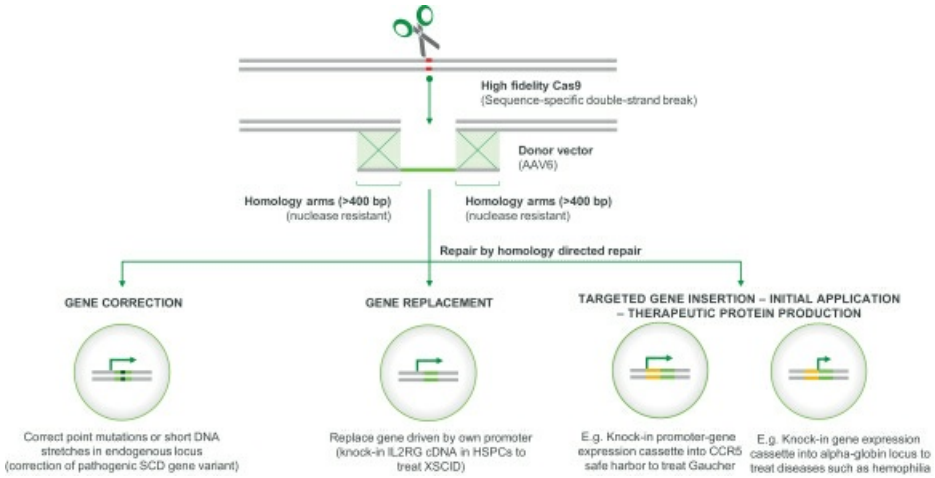
- **Direct targeting and correction of genetic lesions:** We harness HDR to replace the disease-causing mutation or the entire disease-causing gene with the normal, wild-type genetic sequence. This is in contrast to first generation gene editing approaches that have focused on knocking-out genes.
- **Efficiency of targeted gene integration:** In our GPH101 sickle cell gene correction program, we have demonstrated up to approximately 70% gene correction efficiency in hematopoietic stem and progenitor cells (HSPCs) in *ex vivo* studies. In gene replacement and targeted gene insertion applications, we have consistently demonstrated efficiencies of approximately 30-50% in HSPCs across a range of gene targets and templates. We believe these efficiencies are above the curative threshold for a broad array of indications, including SCD. Prior to the development of our gene integration platform efficiencies using HDR in HSPCs were approximately 10%.



- **Breadth of applications:** We can replace genes of up to 4 kilobases (kb) allowing us to correct not only single point mutations but also multiple mutations within the same gene, and to address gene deletions. We can also precisely insert genes under control of a native promoter for naturally regulated expression, into a safe harbor location under the control of an exogenous promoter, or under the control of a lineage specific cellular promoter. For gene insertion, we are initially applying our technology for permanent therapeutic protein production in HSCs. We believe our approach has many additional applications such as engineering effector cells and expressing therapeutic proteins in non-HSC cell types.
- **Uniquely suited to expand the patient population eligible for potential one-time curative HSC therapies:** We believe that the high efficiency and precision of our targeted gene integration platform could potentially reduce threshold bone marrow engraftment levels. This could potentially obviate the need for full chemotherapeutic myeloablative bone marrow conditioning (the current standard for allo-HSCT and most gene editing and gene therapy approaches in development). In addition, our approach avoids the theoretical risk of insertional oncogenesis from integrating viral vectors and incorporates a high fidelity CRISPR-based nuclease, for potentially improved safety. Pairing these advantages with targeted and safer bone marrow conditioning could bring HSC-based curative therapies to much larger numbers of patients.



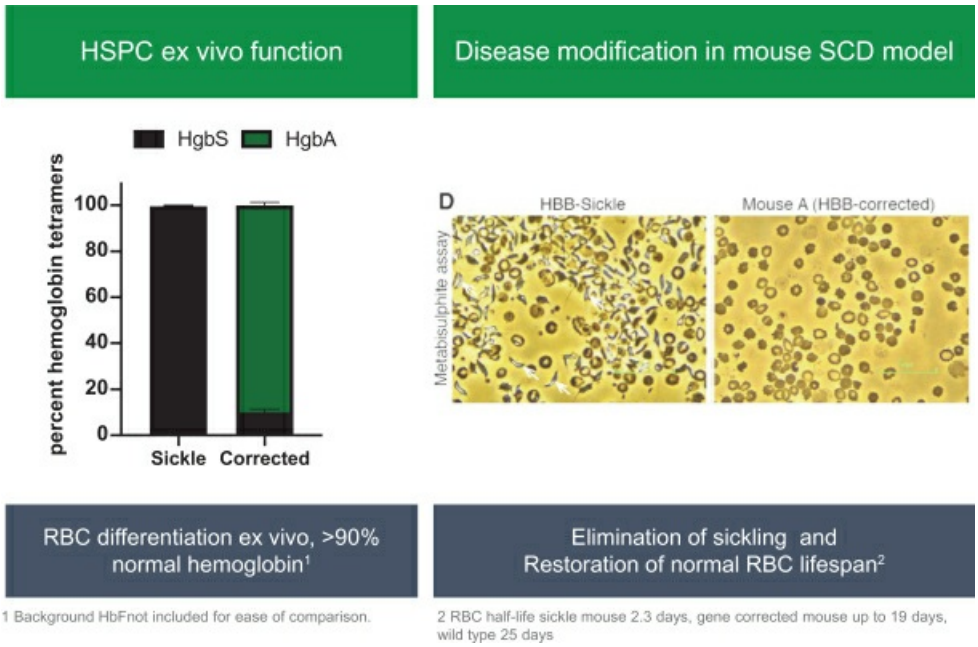
We are applying our technology in three settings: Gene Correction, Gene Replacement, and Targeted Gene Insertion.



Gene Correction

Our approach allows us to precisely correct pathogenic genes by directly targeting and correcting the specific disease-causing mutation to restore the normal, wild-type sequence.

We are developing GPH101, our lead product candidate for SCD, which is designed to directly correct the genetic mutation responsible for SCD. The mortality and morbidity associated with SCD, all caused by a single mutation, has made curing SCD a dream of many clinicians. Multiple genetic therapies are in development to address SCD, but due to technical limitations, these therapies are primarily focused on expressing alternate hemoglobin genes such as fetal hemoglobin or a transgenic hemoglobin. Our approach is the first in industry to directly correct the SCD-causing mutation to restore normal adult hemoglobin expression. Under IND-enabling GMP manufacturing conditions, we can precisely correct the SCD mutation in over 55% of treated cells, which we believe can achieve the threshold required to cure patients (engraftment of 20% corrected cells). These treated HSPCs are fully functional and can engraft *in vivo* in a humanized mouse, and can produce functionally normal red blood cells expressing normal adult hemoglobin *ex vivo.* Furthermore, we have demonstrated in a mouse model of SCD that our approach significantly increased normal HbA expression, extended red blood cell (RBC) lifespan from two days in sickle mice to up to 19 days in gene corrected mice, and eliminated RBC sickling. We believe this data supports the curative potential of our approach. We have received clearance of our IND and intend to enroll the first patient in a Phase 1/2 trial of GPH101 in .



Gene Replacement

Our gene replacement approach allows us to replace dysfunctional genes with a new normal copy of an entire gene at its normal location in the chromosome.

We are developing GPH201 for the treatment of XSCID, a rare, life-threatening disease where multiple mutations in a single gene (IL2RG) prevent normal immune system function. In preclinical studies, we demonstrated that GPH201 treatment of HPSCs from healthy donors led to a consistent rate of IL2RG gene replacement of greater than 40%. Furthermore, treatment of HSPCs from an XSCID patient led to a significant increase in the number of T cells and natural killer (NK) cells, in *in vitro* differentiation assays and in a mouse model, consistent with a reversal of the XSCID phenotype. We believe our gene replacement approach leading to normal regulated expression of the IL2RG gene could be an optimal cure for XSCID. We believe that the survival advantage of the progeny of gene edited cells combined with our high efficiency of gene replacement could enable patients to benefit from GPH201 without undergoing chemotherapy-based conditioning. We have an agreement to investigate the potential use of a clinical-stage non-genotoxic HSC targeted antibody-based bone-marrow conditioning (non-genotoxic HSC targeted conditioning) regimen with GPH201. We believe that GPH201 will generate preliminary data on combining our autologous HSC therapies with non-genotoxic HSC targeted conditioning, and our clinical experience could accelerate our ability to use non-genotoxic HSC targeted conditioning with our other product candidates.

Targeted Gene Insertion

Our technology enables the targeted insertion of entire gene cassettes into chosen chromosomal locations. We believe that this could have broad therapeutic applications by allowing for permanent production of

therapeutic proteins and enzymes, in specific cell lineages, and from targeted genomic locations. This prevents the variability in gene expression, and the potential risk of insertional oncogenesis which are limitations of random gene integration approaches using lentiviral vectors (LVV). Permanent therapeutic protein production applications of HSC targeted integration include expression of proteins and enzymes in target organs including the central nervous system (CNS) by tissue resident HSC-derived myeloid cells, as well as efficient systemic delivery of secreted proteins in the circulation. Potential applications include enzyme replacement for metabolic disease, CNS delivery of therapeutic proteins or antibodies for neurodegenerative diseases, and production of plasma proteins for coagulation and complement disorders.

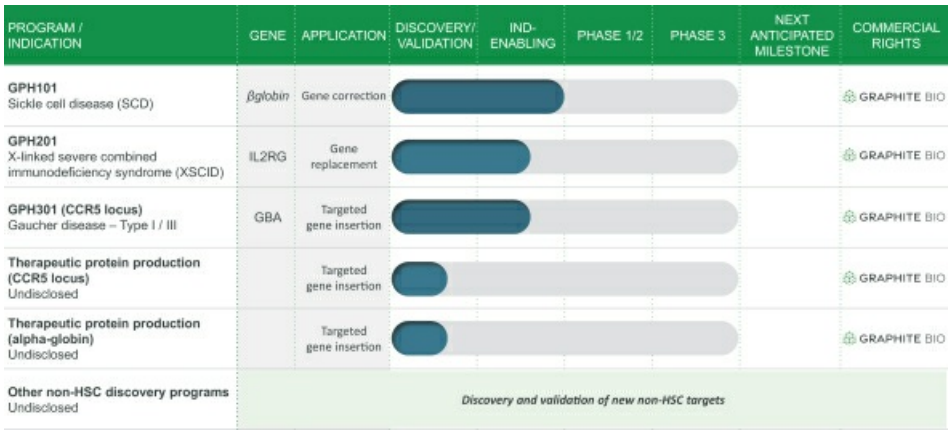
We currently harness two genomic locations for targeted insertion, the CCR5 safe harbor locus and the alpha globin locus:

Our lead product candidate from our CCR5 locus technology is GPH301, which we are developing for the treatment of Gaucher disease. With GPH301, we are inserting a functional copy of the GCase gene into the CCR5 chromosomal locus. This locus is known as a "safe harbor" both because of the lack of deleterious effects associated with gene insertions that occur there and because the expression of inserted genes can be reliably and precisely controlled by regulatory elements inserted together with the gene of interest. We use a lineage specific promoter so that GCase expression is limited to monocytes and macrophages which can migrate into tissues including crossing the blood brain barrier into the CNS. We inserted GCase into approximately 35% of targeted CCR5 alleles in HSPCs (resulting in ~50% of cells having at least one allele targeted) which subsequently engrafted, differentiated, and expressed GCase from macrophages at levels which could lead to a functional cure. This same approach can be used for therapeutic protein production in many other diseases including other lysosomal storage diseases. We believe that proof of concept in Gaucher can accelerate development of a CCR5 safe harbor protein production pipeline. We believe there are significant synergies and regulatory efficiencies because these programs will use the same RNA guide and preclinical safety assessment.

Our other approach for therapeutic protein production harnesses the alpha-globin locus, which uses the alpha-globin promoter to express high protein levels from the red blood cell lineage and normalize plasma protein levels to potentially develop HSC-based cures and treatments for additional indications.

We intend to pursue applications of our technology platform to develop potential therapies for a number of serious diseases. Our high efficiency gene editing technology has been shown using human cells and/or animal models to be applicable to a broad range of HSC-based indications (e.g. MPS1, Krabbe, beta-thalassemia) as well as other tissues, such as airway stem cells (cystic fibrosis), neural stem cells, pluripotent stem cells and keratinocytes (wound healing). We intend to investigate the potential of developing therapies for other diseases based on these findings.

Our Pipeline



Our Team and Investors

Our team is led by executives who have deep experience in drug development and company-building in the biopharmaceutical industry. Josh Lehrer, M.D., our Chief Executive Officer, previously served as chief medical officer at Global Blood Therapeutics (GBT), where he led development for the marketed SCD treatment Oxbryta™ from pre-IND stages through its commercial launch. Prior to GBT, he served in clinical roles at Genentech and as a practicing cardiologist at Stanford. Katherine Stultz, our Chief Operating Officer, has extensive experience in developing brands and building teams, as a global project leader and general manager at Celgene and in early commercialization roles at Eli Lilly. Jerry Cacia, our Chief Technical Officer, most recently served as head of global technical development at Roche/Genentech, where he supported a pipeline that included over 80 new molecular entities and more than 100 development projects in various stages, including a number of cell and gene therapies. Philip Gutry, our Chief Business Officer and Head of Finance & Investor Relations, previously served as Chief Business Officer at Kronos Bio and in senior business development and finance roles at Regeneron, MPM Capital, and Gilead. We are building a broader team that is passionate about our mission of urgently translating groundbreaking science to transform lives. Our people function is led by SVP Julia Tran, a three-time executive with more than 20 years of experience in building and growing companies in the biotechnology industry including Amyris, Inc., CV Therapeutics, Inc. and Millennium Pharmaceuticals Inc. and in technology companies including vArmour Networks, SilverTail Systems and most recently Blue Lava where she was a founder, Chief Operating Officer and Chief Community Officer.

Since our inception, we have raised approximately $197.7 million in funding from leading investors, including Cormorant Asset Management, Deerfield Management Company, Federated Hermes Kaufmann Funds, Fidelity Management & Research Company, Janus Henderson Investors, Logos Capital, OrbiMed, Perceptive Advisors, RA Capital, Rock Springs Capital, Samsara BioCapital, Surveyor Capital (a Citadel company), Venrock Healthcare Capital Partners, and our founding investor Versant Ventures. Stanford University also participated in our Series B preferred stock financing in March 2021.

Our Strategy

We are a next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to cure a wide range of serious and life-threatening diseases. Our goal is to

advance a portfolio of one-time curative therapies which can ultimately be administered in the outpatient setting. The key components of our strategy are as follows:

- Rapidly demonstrate clinical proof-of-concept for gene correction with our lead product candidate, GPH101, for the treatment of sickle disease.
- Expeditiously advance the gene replacement application of our technology with GPH201 for the treatment of XSCID.
- Establish the broad potential of targeted gene insertion with GPH301 for the treatment of Gaucher disease.
- Expand the patient population and indications eligible for one-time curative HSC therapies by harnessing industry advances in non-genotoxic HSC targeted conditioning regimens.
- Leverage high efficiency targeted gene integration in other cell types.
- Continue to optimize and expand our next-generation gene editing technology to reinforce our leadership in targeted gene integration.
- Evaluate potential strategic collaborations to maximize the broad therapeutic potential of our technology and product candidates.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. These risks include, but are not limited to, the following:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- Our limited operating history may make it difficult for you to evaluate the performance of our business to date and to assess our future viability.
- We have never generated revenue from product sales, may never generate any revenue from product sales and may never become profitable.
- Even if this offering is successful, we will need substantial additional funding. If we are unable to raise capital when needed on acceptable terms, or at all, we would be forced to delay, reduce, or terminate our research and product development programs, future commercialization efforts or other operations.
- We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including the COVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business.
- We are very early in our development efforts. Other than GPH101, which is in early clinical development, all of our product candidates are still in preclinical development or earlier stages and it will be many years before we or our collaborators commercialize a product candidate, if ever. If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our gene editing technology is not approved for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics may never lead to marketable products.
- If serious adverse events, undesirable side effects, or unexpected characteristics are identified with respect to our product candidates, we may need to abandon or limit our clinical development or commercialization of those product candidates.

- 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, less expensive or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize our product candidates.
- Adverse public perception of genetic medicines and gene editing in particular, may negatively impact regulatory approval of, and/or demand for, our potential products, if approved.
- We contract with third parties for the manufacture of materials for our research programs and preclinical studies and expect to continue to do so for clinical trials and for commercialization of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any products that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or timelines, which could delay, prevent, or impair our development or commercialization efforts.
- If we are unable to obtain and maintain patent and other intellectual property protection for any product candidates we develop and for our gene editing platform technology, or if the scope of the patent and other intellectual property 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 gene editing platform technology may be adversely affected.
- Our rights to develop and commercialize our gene editing platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.
- The intellectual property landscape around gene 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 may prevent, delay or otherwise interfere with our product discovery and development efforts.
- Our owned and in-licensed patents and other intellectual property may be subject to priority disputes or inventorship disputes or we may be subject to claims that we have infringed, misappropriated or otherwise violated the intellectual property of a third party and similar proceedings. If we or our licensor are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of our product candidates, which could have a material adverse impact on our business.

Corporate History and Information

We were incorporated in Ontario, Canada on June 1, 2017 as Longbow Therapeutics Inc. and were reincorporated in the State of Delaware in October 2019. In February 2020, we changed our name to Integral Medicines, Inc. and in August 2020, we changed our name to Graphite Bio, Inc. Research and development of our initial technology ceased at the end of 2018 and we did not have any significant operations or any research and development activities in 2019. We began our current research and development activities and operations in 2020.

Our principal executive office is located at 279 East Grand Avenue, Suite 430, South San Francisco, CA 94080, and our telephone number is (650) 484-0886. Our website address is https://graphitebio.com/. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (JOBS Act). As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements in this prospectus and only two years of related "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our periodic reports and registration statements, including this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (SOX);
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements, and registration statements, including in this prospectus; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these exemptions for up to five years from the date of effectiveness of this registration statement or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission (SEC), which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (1) are no longer an emerging growth company or (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

THE OFFERING

Common stock offered by us	shares.
Underwriters' over-allotment option	shares.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise their over-allotment option to purchase additional shares in full).
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million (or $ million if the underwriters exercise their over-allotment option to purchase additional shares in full) assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We currently intend to use the net proceeds from this offering, including our existing cash and cash equivalents, to fund our clinical development of GPH101 for the treatment of SCD, GPH201 for the treatment of XSCID and GPH301 for the treatment of Gaucher disease, to fund our current discovery programs in CCR5 and alpha globin, and for working capital and general corporate purposes. See the section titled "Use of Proceeds" for additional information.
Risk factors	See the section titled "Risk Factors" and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
Proposed Nasdaq symbol	"GRPH"

The number of shares of our common stock to be outstanding immediately after this offering is based on 99,811,239 shares of common stock outstanding as of December 31, 2020, including (i) our restricted common stock subject to vesting and (ii) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock (including shares of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock issued in February 2021 and March 2021, respectively) into an aggregate of 74,812,432 shares of our common stock immediately prior to the completion of this offering), and excludes:

- 746,000 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2020, with a weighted-average exercise price of $0.12 per share;
- 5,329,944 shares of our common stock issuable upon the exercise of outstanding stock options granted after December 31, 2020, with a weighted-average exercise price of $2.14 per share;
- 5,020,152 shares of our common stock reserved for future issuance under our 2020 Stock Option and Grant Plan (2020 Plan), as of December 31, 2020;

- shares of our common stock reserved for future issuance under our 2021 Stock Option and Incentive Plan (2021 Plan), which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 Plan; and
- shares of our common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan (2021 ESPP), which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 ESPP.

Unless we specifically state otherwise or the context otherwise requires, this prospectus reflects and assumes the following:

- a 1 -for- reverse stock split of our capital stock effected on , 2021;
- the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 74,812,432 shares of our common stock immediately prior to the completion of this offering;
- no exercise of the outstanding options described above;
- no exercise by the underwriters of their over-allotment option; and
- the adoption, filing and effectiveness of our amended and restated certificate of incorporation and our amended and restated bylaws, which will occur immediately prior to the completion of this offering.

SUMMARY FINANCIAL DATA

The following tables set forth our summary statements of operations and comprehensive loss data for the years ended December 31, 2019 and 2020 and our summary balance sheet data as of December 31, 2020, and have been derived from our audited financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the following summary financial data together with the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus and our financial statements and the related notes included elsewhere in this prospectus. The summary financial data included in this section are not intended to replace the audited financial statements and the related notes included elsewhere in this prospectus and are qualified in their entirety by the financial statements and the related notes included elsewhere in this prospectus.

	Year Ended December 31,	
	2019	2020
	(in thousands, except share and per share amounts)	
Statements of Operations and Comprehensive Loss Data:		
Operating expenses:		
Research and development	$ —	$ 9,123
General and administrative	29	4,377
Total operating expenses	29	13,500
Loss from operations	(29)	(13,500)
Other income (expense), net:		
Related party convertible note interest expense	(80)	(40)
Change in fair value of the redeemable convertible preferred stock tranche liabilities	—	(54,833)
Total operating income (expense), net	(80)	(54,873)
Net loss and comprehensive loss	$ (109)	$ (68,373)
Net loss per share attributable to common stockholders, basic and diluted[1]	$(109,000)	$ (12.31)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted[1]	1	5,554,899
Pro forma net loss per share attributable to common stockholders, basic and diluted[2]		$ (0.38)
Weighted-average shares outstanding used in computing pro forma net loss per share attributable to common stockholders, basic and diluted[2]		35,574,844

(1) See Notes 2 and 11 to our financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(2) See the section titled "Management's Discussion and Analysis of Financial Conditions and Results of Operations—Unaudited Pro Forma Information" for an explanation of the calculation of our basic and diluted pro forma net loss per share, and the weighted-average number of shares outstanding used in the computation of the per share amounts.

	As of December 31, 2020		
	Actual	Pro Forma(1) (in thousands) (unaudited)	Pro Forma As Adjusted(2)(3) (unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 19,782	$	$
Working capital(4)	(10,945)		
Total assets	22,564		
Redeemable convertible preferred stock	55,608		
Additional paid-in capital	5,183		
Accumulated deficit	(70,591)		
Total stockholders' deficit	(65,408)		

(1) The pro forma column in the balance sheet data table above gives effect to (i) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of December 31, 2020 into an aggregate of 30,019,945 shares of our common stock immediately prior to the completion of this offering; (ii) our receipt of aggregate net proceeds of approximately $165.7 million from the sale of shares of our redeemable convertible preferred stock in February 2021 and March 2021 and the automatic conversion of these shares into an aggregate of 44,792,487 shares of our common stock immediately prior to the completion of this offering and (iii) the adoption, filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the completion of this offering.

(2) The pro forma as adjusted column in the balance sheet data table above gives effect to (i) the pro forma adjustments set forth in footnote (1) above; and (ii) the sale of shares of common stock in this offering at the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the amount of each of our cash and cash equivalents, working capital, total assets and total stockholders' deficit by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Similarly, each increase or decrease of 1.0 million in the number of shares we are offering would increase or decrease, as applicable, the amount of each of our cash and cash equivalents, working capital, total assets and total stockholders' deficit by approximately $ million, based on the assumed initial public offering price per share, the midpoint of the price range as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

(4) We define working capital as current assets less current liabilities. See our consolidated financial statements and the related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the events or developments described below were to occur, our business, financial condition, results of operations and prospects could be materially and adversely affected, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Our Financial Position, Limited Operating History and Need for Additional Capital

We have incurred significant losses since our inception, we expect to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability.

Since our inception, we have incurred significant net losses, have not generated any revenue from product sales to date and have financed our operations principally through private placements of our redeemable convertible preferred stock. Our net loss was $0.1 million and $68.4 million for the years ended December 31, 2019 and 2020, respectively. As of December 31, 2020, we had an accumulated deficit of $70.6 million. We expect to continue to incur significant and increasing losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. We anticipate that our expenses will increase substantially if and as we:

- initiate and conduct our clinical trials for GPH101 and our current and future product candidates that we may identify and develop;
- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- hire additional research and development and clinical personnel;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- establish our manufacturing capability, including developing our contract development and manufacturing relationships, and should we decide to do so, building and maintaining a commercial-scale current Good Manufacturing Practices (cGMP), manufacturing facility;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- further develop our gene editing platform;
- add operational, financial, and management information systems and personnel;
- acquire or in-license product candidates, intellectual property and technologies; and
- operate as a public company.

To date, we have not initiated a clinical trial for any product candidate and expect that it will be many years, if ever, before we have a product candidate ready for commercialization, if approved. To become and remain profitable, we must develop and eventually commercialize products with significant market potential. This will

require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those products for which we may obtain marketing approval, obtaining market acceptance for such products and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenue in an amount sufficient to achieve profitability. Most of our programs are currently only in the preclinical testing stage and early clinical development stage, and we expect to commence clinical trials for GPH101 in 2021. Because of the numerous risks and uncertainties associated with developing gene editing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if ever. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and our stock price and could impair our ability to raise capital, maintain and fund our research and development efforts, expand our business, or continue our operations. A decline in the value of our Company could also cause you to lose all or part of your investment.

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

We are an early-stage company. We were founded in 2017 and commenced operations in 2020. Our operations to date have been limited to organizing and staffing our Company, business planning, raising capital, acquiring and developing our platform and technology, identifying potential product candidates, establishing and maintaining our intellectual property portfolio, undertaking preclinical studies and preparing for clinical trials. Other than GPH101, which is in early clinical development, all of our research programs are still in the preclinical or research stage of development, and their risk of failure is high. We have not demonstrated an ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop a new product from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about the likelihood of our future success or viability may not be as accurate as they could be if we had a longer operating history.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our very short history as an operating company makes any assessment of the likelihood of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as a new business, we may encounter other unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have never generated revenue from product sales, may never generate any revenue from product sales and may never become profitable.

Our ability to generate revenue from product sales and achieve profitability, if ever, depends on our ability, alone or with collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our current product candidates and any product candidates we may identify for development. We do not anticipate generating revenues from product sales for the next several years, if ever.

Even if one or more of the product candidates we develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could

increase beyond expectations if we are required by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved product candidates, we may not become profitable and may need to obtain additional funding to continue operations.

Even if this offering is successful, we will need substantial additional funding. If we are unable to raise capital when needed on acceptable terms, or at all, we would be forced to delay, reduce, or terminate our research and product development programs, future commercialization efforts or other operations.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate and conduct clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Other unanticipated costs may also arise. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce, or eliminate our research and product development programs, future commercialization efforts or other operations.

As of December 31, 2020, our cash, cash equivalents, and marketable securities were $19.8 million. We expect that the net proceeds from this offering, together with our existing cash, cash equivalents, and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. However, our operating plan may change as a result of factors currently unknown to us, and we may need to seek funding sooner than planned. Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, results and costs of our planned clinical trials of GPH101 and other product candidates that we may identify and develop;
- the costs, timing, and outcome of regulatory review of the product candidates we develop;
- the costs of continuing to build our gene editing platform;
- the timing, scope, progress, results, and costs of discovery, preclinical development and formulation development for the product candidates we develop;
- the costs of preparing, filing, and prosecuting patent applications, establishing, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, distribution, coverage and reimbursement for any product candidates for which we receive regulatory approval;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- our ability to establish and maintain additional collaborations, licenses or other similar arrangements on favorable terms, if at all;
- the success of any collaborations that we may establish and of our license agreements;
- the continued effect of the COVID-19 pandemic on our business;

- the extent to which we acquire or in-license product candidates, intellectual property and technologies; and
- the costs of operating as a public company.

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, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products 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. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We have no committed sources of additional capital and, 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 our product candidates or other research and development initiatives. Without sufficient funding, our license agreements and any future collaboration agreements may also be terminated if we are unable to meet the payment or other obligations under such agreements.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt 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, declaring dividends, and possibly other restrictions.

If we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates we develop, or we may have to grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock. 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 may be subject to adverse legislative or regulatory tax changes that could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

As of December 31, 2020, we had U.S. federal net operating loss carryforwards of $10.8 million (which are not subject to expiration) and state net operating loss carryforwards of $29,000, (which begin to expire in various amounts in 2039). Our ability to use our U.S. federal and state net operating losses to offset potential future taxable income and reduce income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses.

Under current law, unused U.S. federal net operating losses generated in taxable years beginning after December 31, 2017 are not subject to expiration and may be carried forward indefinitely. For taxable years beginning after December 31, 2020, however, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in such taxable years. In addition, both our current and our future unused U.S. federal net operating losses and tax credits may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a rolling three-year period. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside our control. Our net operating losses and tax credits may also be impaired or restricted under state law.

We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including theCOVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business.

Significant outbreaks of contagious diseases, and other adverse public health developments, could have a material impact on our business operations and operating results. For example, the spread of COVID-19 has affected segments of the global economy and could affect our operations. As a result of the COVID-19 pandemic or similar public health crises that may arise, we may experience disruptions that could adversely impact our operations, research and development, including preclinical studies, clinical trials and manufacturing activities, including:

- delays or disruptions in clinical trials that we may be conducting, including patient screening, patient enrollment, patient dosing, clinical trial site activation, and study monitoring;
- delays or disruptions in preclinical experiments and IND-enabling and clinical trial application-enabling studies due to restrictions related to our staff being on site;
- interruption or delays in the operations of the FDA, the EMA and comparable foreign regulatory agencies;
- interruption of, or delays in, receiving, supplies of drug substance and drug product from our CMOs or delays or disruptions in our pre-clinical experiments or clinical trials performed by CROs due to staffing shortages, production and research slowdowns or stoppages and disruptions in delivery systems or research;
- limitations imposed on our business operations by local, state, or federal authorities to address such pandemics or similar public health crises could impact our ability to conduct preclinical or clinical activities, including conducting IND-enabling studies or our ability to select future development candidates;
- the impact of the COVID-19 pandemic on our corporate culture; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, cyber security and data accessibility, or

communication or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors.

For example and in light of the ongoing COVID-19 pandemic, our partner Stanford was delayed in making anIND-filing. In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic, and we may face similar volatility in our stock price.

We cannot predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, financial condition, our results of operations and prospects.

For additional information regarding the impact of the COVID-19 pandemic on our Company, see the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations—Business Impact of COVID-19 Pandemic."

Risks Related to Discovery, Development, and Commercialization

We are very early in our development efforts. Other than GPH101, which is in early clinical development, all of our product candidates are still in preclinical development or earlier stages and it will be many years before we or our collaborators commercialize a product candidate, if ever. If we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have focused our research and development efforts to date on gene editing technology, identifying our initial targeted disease indications and our initial product candidates. We have not achieved preclinical proof of concept for the majority of our programs and there is no guarantee that we will achieve it for these programs. Our future success depends heavily on the successful development of our gene editing product candidates. To date, we have invested substantially all of our efforts and financial resources in building our gene editing platform, and the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur.

Commencing clinical trials in the United States is also subject to acceptance by the FDA of our INDs, and finalizing the trial design based on discussions with the FDA and other regulatory authorities. 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 clinical trials 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. There are equivalent processes and risks applicable to clinical trial applications in other countries, including in Europe.

Commercialization of our product candidates will require additional preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; obtaining manufacturing supply, capacity and expertise; building of a commercial organization; and significant marketing efforts. The success of product candidates we identify and develop will depend on many factors, including the following:

- sufficiency of our financial and other resources to complete the necessary preclinical studies,IND-enabling studies, and clinical trials;

- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization (CMO), or by us;
- obtaining and maintaining patent, trade secret, and other intellectual property protection and non-patent exclusivity for our products;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile of the products following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- supplying the product that is cost-effective and acceptable to the pricing or reimbursement authorities in different countries.

If we do not successfully achieve one or more of these activities in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Our gene editing technology is not approved for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics may never lead to marketable products.

We are focused on developing curative medicines utilizing the CRISPR gene editing technology. CRISPR-based gene editing technologies are relatively new and their therapeutic utility is largely unproven. Our successful development of products will require solving a number of issues, including developing or obtaining technologies to safely deliver a therapeutic agent into target cells within the human body or engineer human cells while outside of the body such that the modified cells can have a therapeutic effect when delivered to the patient, optimizing the efficacy and specificity of such products, and ensuring and demonstrating the therapeutic selectivity, efficacy, potency, purity and safety of such products. There can be no assurance we will be successful in solving any or all of these issues. Indeed, no gene editing cell therapy has been approved in the United States, the European Union (EU), other countries or other key jurisdictions. Accordingly, the potential to successfully obtain approval for any of our CRISPR technology-based therapies remains unproven.

Our future success also is highly dependent on the successful development of CRISPR-based gene editing technologies and therapeutic applications for the indications on which we have focused our ongoing research and development efforts. We may decide to alter or abandon these programs as new data become available and we gain experience in developing CRISPR-based therapeutics. We cannot be sure that our gene editing technologies will yield satisfactory products that are safe and effective, sufficiently pure or potent, manufacturable, scalable or profitable in our selected indications.

We are subject to additional development challenges and risks due to the novel nature of our gene editing technology.

Because our *in vivo* technology potentially involves gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that other gene editing therapeutics and gene therapies face, including:

- regulatory guidance regarding the requirements governing gene and gene editing therapy products have changed and may continue to change in the future;
- to date, only a limited number of products that involve in vivo gene transfer have been approved globally;
- improper modulation of a gene sequence, including unintended editing events or insertion of a sequence into certain locations in a patient's chromosome, could lead to cancer, other aberrantly functioning cells or other diseases, including death;
- corrective expression of a missing protein in patients' cells could result in the protein being recognized as foreign, and lead to a sustained immunological reaction against the expressed protein or expressing cells, which could be severe or life-threatening; and
- regulatory agencies may require extended follow-up observation periods of patients who receive treatment using gene editing products including, for example, the FDA's recommended 15-year follow-up observation period for these patients, and we will need to adopt such observation periods for our product candidates if required by the relevant regulatory agency, which could vary by country or region.

Further, because our *ex vivo* product candidates involve editing human cells and then delivering modified cells to patients, we are subject to many of the challenges and risks that engineered cell therapies face. For example, clinical trials using engineered cell-based gene therapies may require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

We may not be successful in our efforts to identify and develop potential product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.

The success of our business depends primarily upon our ability to identify, develop, and commercialize product candidates based on our gene editing platform. Our research programs may fail to identify potential product candidates for clinical development for a number of reasons: our research methodology may be unsuccessful in identifying potential product candidates; our potential product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies; they may not show promising signals of therapeutic effect in such experiments or studies; or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable, or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our research or development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations, and prospects and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful, which would be costly and time-consuming.

If serious adverse events, undesirable side effects, or unexpected characteristics are identified with respect to our product candidates, we may need to abandon or limit our clinical development or commercialization of those product candidates.

To date, we have not evaluated any product candidates in human clinical trials. It is impossible to predict when or if any product candidates we develop, including our product candidates, GPH101, GPH201 and

GPH301, will ultimately 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 gene editing technologies will not cause severe or undesirable side effects.

A significant potential risk in any gene editing product is that the edit will be“off-target” and cause serious adverse events, undesirable side effects, 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. We cannot be certain that off-target editing will not occur in any of our clinical studies. 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 components of products used to carry the genetic material. If any adverse events or side effects are caused by any product candidate we develop and test, the administration process or related procedures, our clinical trials could be delayed, suspended or terminated.

Viral vectors, including AAV, which are relatively new approaches used for disease treatment, also have known side effects, and for which additional risks could develop in the future. In past clinical trials that were conducted by others with non-AAV vectors, significant side effects were caused by gene therapy treatments, including reported cases of myelodysplasia, leukemia and death. Other potential side effects could include an immunologic reaction and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. If the vectors we use demonstrate a similar side effect, or other adverse events, we may be required to halt or delay further clinical development of any potential product candidates. Furthermore, the FDA has stated that LVV possess characteristics that may pose high risks of delayed adverse events. Such delayed adverse events may also occur in other viral vectors, including AAV vectors.

In addition to side effects and adverse events caused by our product candidates, the conditioning, administration process or related procedures which may be used to condition a patient for gene therapy treatment also can cause adverse side effects and adverse events. A gene therapy patient is generally administered cytotoxic drugs to remove stem cells from the bone marrow to create sufficient space in the bone marrow for the modified stem cells to engraft and produce new cells. This procedure compromises the patient’s immune system, and conditioning regimens have been associated with adverse events in clinical trial participants.

If any product candidates we develop are associated with serious adverse events, undesirable side effects, or unexpected characteristics, 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 have a material adverse effect on our business, financial condition, results of operations, and prospects. Many product candidates, including gene therapy 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.

If we are unable to demonstrate that any of the above adverse events were caused by factors other than our product candidate, the FDA, 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. 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 and could have a material adverse effect on our business, financial condition, result 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 Risk Evaluation and Mitigation Strategy (REMS), to ensure that the benefits of

treatment with such product candidate outweighs the risks for each potential patient, which 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. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we develop, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label or limit the approved use of such product candidate;
- we may be required to conduct additional clinical trials;
- 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 any of our product candidates and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates may be developed. If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities and our receipt of necessary regulatory approvals could be delayed or prevented.

We 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, the EMA or other analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy, or gene editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of our product candidates may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;

- perceived risks and benefits of gene editing as a therapeutic approach;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients, especially for those conditions which have small patient pools.

In addition, the COVID-19 pandemic may affect the timing of our planned clinical trials. Clinical trial activities, including patient enrollment and data collection, are dependent upon global clinical trial sites which have been and continue to be adversely affected by the COVID-19 pandemic. For example, as the global healthcare community responded to the fluctuations in COVID-19 cases and hospitalizations, many hospitals, including those operating as clinical trial sites for other ongoing trials, temporarily paused elective procedures, which included dosing of new patients with investigational products. Additionally, the COVID-19 pandemic may cause delays in data collection and monitoring activities, which may present data integrity challenges or require modifications to our planned clinical trial protocol.

In addition, 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;
- difficulty in locating 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 and of gene editing technologies.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our Company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

If we are unable to successfully identify patients who are likely to benefit from therapy with our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of any products we may develop.

Our success may depend, in part, on our ability to identify patients who are likely to benefit from therapy with our product candidates, which requires those potential patients to have their DNA analyzed for the presence or absence of a particular sequence. If we, or any third parties that we engage to assist us, are unable to successfully identify such patients, or experience delays in doing so, then:

- our ability to develop our product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials; and
- we may not realize the full commercial potential of any product candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our product candidates.

As a result of these factors, we may be unable to successfully develop and realize the commercial potential of our product candidates, and our business, financial condition, results of operations, and prospects would be materially adversely affected.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we develop, and our ability to generate revenue will be materially impaired.

Any product candidates we develop and the activities associated with their development and commercialization, including their design, testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale, import, export, and distribution, are subject to comprehensive regulation by the FDA, the EMA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third parties to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biological product candidate's safety, purity, and potency. Securing regulatory approval also requires the submission of extensive information about the product manufacturing process, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. 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. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

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 among many potential options. 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 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 have a material adverse effect on our business, financial condition, results of operations, and prospects.

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 in the United States or any other jurisdiction, 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 our product candidates 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 REMS. These regulatory authorities may require labeling that includes precautions or contraindications 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 our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially adversely affect our business, financial condition, results of operations, and prospects.

Marketing approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. 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 candidate testing and validation and additional administrative review periods. Seeking regulatory approval outside the United States could result in difficulties and 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 product candidates in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including 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 our product candidates will be unrealized.

Our product candidates may fail to achieve the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Ethical, social, and legal concerns about genetic medicines generally and gene editing technologies specifically could result in additional regulations restricting or prohibiting the marketing of our product candidates. Even if our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians,

patients, third-party payors, and others in the medical community. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages compared to alternative treatments;
- the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authorities;
- the ability to offer our products for sale at cost-effective or competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, the EMA, or other regulatory agencies;
- public attitudes regarding genetic medicine generally and gene editing technologies specifically;
- the willingness of the target patient population to try novel therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient's gene;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength and effectiveness of sales, marketing and distribution efforts;
- sufficient third-party coverage and adequate reimbursement, including the ability to supply product that is cost-effective and acceptable to the pricing or reimbursement authorities in different countries; and
- the prevalence and severity of any side effects.

Even if any of our product candidates obtain regulatory approval, such products may not achieve an adequate level of acceptance, we may not generate or derive sufficient product revenues, and we may not become profitable.

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, less expensive or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize our product candidates.

The development and commercialization of new drug 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 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.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches.

There are several other companies in pre-clinical or clinical development utilizing CRISPR nuclease technology, including AVROBio, Inc., Beam Therapeutics Inc., bluebird bio, Inc., CRISPR Therapeutics, Inc., Editas Medicine, Inc., Freeline Therapeutics, Homology Medicines, Inc., Intellia Therapeutics, Inc., Mustang Bio, Inc., Orchard Therapeutics plc and Sangamo BioSciences.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates. This may include other types of therapies, such as small molecule, antibody, and/or protein therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, may 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 product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any product candidates that we may develop or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates 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 uneconomical or obsolete, and we may not be successful in marketing our product candidates 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 product candidates that we may develop and commercialize.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have limited experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved products for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the benefits of prescribing any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- restricted or closed distribution channels that make it difficult to distribute our product candidates to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

Our potential therapeutic products involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public understanding and acceptance of the use of gene editing therapy for the prevention or treatment of human diseases. Public perception and related media coverage of potential gene therapy-related efficacy or safety issues, including adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to gene editing, may adversely influence the willingness of subjects to participate in clinical trials, or if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, health care providers and third-party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and potentially personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Further, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies.

In addition, responses by federal and state agencies, congressional committees and foreign governments to negative public perception, ethical concerns or financial considerations may result in new legislation, regulations, or medical standards, such as stricter labeling requirements, that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. 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. Based on these and other factors, health care providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

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 our product candidates. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to product candidates we identify 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 identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates. Use of gene editing technology by a third party or government to develop biological agents or products that threaten U.S. national security could similarly result in such negative impacts to us.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new products vary widely from country to country. Some countries require approval of the sale price of a product 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 product in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates we develop, even if any of our product candidates obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government authorities or healthcare programs, private health plans, and other organizations. Government authorities and third-party payors, such as private health plans, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are challenging the prices charged for medical products and requiring that drug companies provide them with predetermined discounts from list prices. Novel medical products, if covered at all, may be subject to enhanced utilization management controls designed to ensure that the products are used only when medically necessary. Such utilization management controls may discourage the prescription or use of a medical product by increasing the administrative burden associated with its prescription or creating coverage uncertainties for prescribers and patients. We cannot be sure that reimbursement will be available for any products that we commercialize and, if reimbursement is available, that the level of reimbursement will be adequate. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA, the EMA or other regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for

products 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 products from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

Due to the novel nature of our technology and the potential for our product candidates 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, as a result of which the pricing and reimbursement of any of our product candidates, 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 develop (e.g., for administration of our product candidate to patients) is also important. Inadequate reimbursement for such services may lead to physician and payor resistance and adversely affect our ability to market or sell our product candidates. In addition, we may need to develop new reimbursement models in order to realize adequate value. 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 a gene editing therapy, 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 government and private 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 of our product candidates will be paid by government authorities, private health plans, and other third-party payors. Payors may not be willing to pay high prices for a single administration. 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. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. 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 of our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

In the United States, no uniform policy exists for coverage and reimbursement for products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided can differ significantly from payor to payor. The process for determining whether a payor will provide coverage

for a product may be separate from the process for setting the reimbursement rate a payor will pay for the product. One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication.

Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Despite our best efforts, our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the EU, pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices of medicinal products for human use. 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 candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the United States and prices generally tend to be significantly lower.

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

We focus our research and product development on treatments for rare genetically defined diseases. Many of our product candidates are expected to target a single mutation; as a result, the relevant patient population may therefore be small. 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 our product candidates, 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 product candidates, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations, and prospects. Additionally, because of the potential that any product candidates we develop could cure a target disease, we may not receive recurring revenues from patients and may deplete the patient population prevalence through curative therapy.

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

Our product candidates 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 are developing generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate 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 unusable products, product recalls, product liability claims, insufficient inventory, or potentially delay progression of our potential IND filings. We may also encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. For example, the current approach of manufacturing AAV vectors may fall short of supplying required number of doses needed for advanced stages of pre-clinical studies or clinical trials, and the FDA may ask us to demonstrate that we have the appropriate manufacturing processes in place to support the higher-dose group in our future pre-clinical studies or clinical trials.

In addition, the FDA, the EMA, and other regulatory authorities may require us to submit samples of any of the 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 sample 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 product recalls. 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 also may encounter problems hiring and retaining the experienced scientific, quality control, and manufacturing personnel needed to manage 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, including for AAV vectors, 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 our current or future product candidates 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 ensure sufficient clinical material for our planned clinical trials and to meet market demand for any product candidates we develop and commercialize.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of our product candidates.

We face an inherent risk of product liability exposure related to the testing in human clinical trials of our product candidates and will face an even greater risk if we commercially sell any products we 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 of our current or future product candidates;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize our product candidates.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any products. 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.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

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 have a material adverse effect on 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 have a material adverse effect on our 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 have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Our Relationships with Third Parties

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

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing, and we expect to rely on third parties to help conduct our planned clinical trials. Any of these third parties may terminate their engagements with us at any time under certain criteria. If we need to enter into alternative arrangements, it may delay our product development activities.

Our reliance on these third parties to conduct clinical trials and for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA, the EMA and other regulatory authorities require us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected.

Although we intend to design the clinical trials for our product candidates, CROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct current and future preclinical studies and future clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with third parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Third parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our

CROs and other third parties, we could be required to repeat, extend the duration of, or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures, which could have a material adverse effect on our business, financial condition, result of operations, and prospects.

We also expect to rely on 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 our product candidates or commercialization of our therapies, producing additional losses and depriving us of potential product revenue.

Dr. Porteus, our co-founder and a member of our board of directors, may have actual or potential conflicts of interest because of his position with Stanford.

Following this offering, Dr. Porteus will continue to serve on our board of directors, our Scientific & Clinical Advisory Board and as our paid consultant and will retain his position and affiliation with Stanford. Furthermore, Dr. Porteus holds shares of our restricted common stock subject to vesting based, among other things, on his continued service to us as a director, employee or consultant. Dr. Porteus' position at Stanford creates, or may create the appearance of, conflicts of interest when we ask Dr. Porteus to make decisions that could have different implications for Stanford than the decisions have for us or for himself, including decisions related to our license of intellectual property rights from Stanford and other contractual relationships we may enter into from time to time with Stanford.

We contract with third parties for the manufacture of materials for our research programs and preclinical studies and expect to continue to do so for clinical trials and for commercialization of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any products that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or timelines, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities at the present time. We currently rely on third-party manufacturers for the manufacture of materials for our research programs and preclinical studies, including our viral vectors, GMP plasmids, RNA guides and Cas9, and expect to continue to rely on third parties, including Stanford, for our planned clinical trials and for commercialization of any product candidates for which we obtain marketing approval. For example, we rely on third parties to manufacture viral vectors. We do not have a long term supply agreement with any of our third-party manufacturers, and we purchase our required supply on a purchase order basis, which means that aside from any binding purchase orders we have from time to time, our third-party manufacturers could cease manufacturing for us or change the terms on which they are willing to continue manufacturing for us at any time.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms for one or more of our material needs. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible failure of the third party to manufacture our product candidates according to our schedule, or at all, including if the third party gives greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets andknow-how;
- 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, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business, financial condition, results of operations, and prospects.

Any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of suppliers or manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. For example, three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

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 manufacturer cannot perform as agreed, we may be required to replace that manufacturer, or we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different third-party manufacturer, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original third-party manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change third-party manufacturers for any reason, we will be required to verify that the new third-party manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new third-party manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third-party manufacturer may possess technology related to the manufacture of our product candidate that such third-party manufacturer owns independently. This would increase our reliance on such third-party manufacturer or require us to obtain a license from such third-party manufacturer in order to have another third-party manufacturer manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

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

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 third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. 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 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.

Collaborations involving our research programs or our product candidates pose numerous risks to us, including the following:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. If a present or future 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.
- Collaborators 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.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such products.
- Collaborators 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.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our therapies or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- Collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.
- Collaborators 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.

- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates we develop.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

If our collaborations do not result in the successful development and commercialization of product candidates, 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 in this prospectus apply to the activities of our collaborators.

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 product candidates we develop that are the subject of these collaborations with us. 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.

If we are not able to establish collaborations on a timely basis, on commercially reasonable terms, or at all, we may have to alter, reduce or delay our development and commercialization plans, or increase our expenditures to fund development or commercialization activities at our own expense.

For some of the product candidates we may develop, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborations and collaborations are complex and time-consuming to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

We may also be restricted under existing collaboration agreements from entering into future collaboration agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators, which further increases competition we face in seeking potential collaborations.

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

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for any product candidates we develop and for our gene editing platform technology, or if the scope of the patent and other intellectual property 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 gene editing platform technology may be adversely affected.

Our commercial success will depend in large part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection of our gene editing platform technology, product candidates and other technology, methods used to manufacture them and methods of treatment, as well as successfully defending our patent and other intellectual property rights against third-party challenges. It is difficult and costly to protect our gene editing platform technology and product candidates, and we may not be able to ensure their protection. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

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 gene editing platform technology and product candidates that are important to our business. If we or our licensor are unable to obtain or maintain patent protection with respect to our gene editing platform technology and our product candidates, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours and our ability to commercialize our product candidates may be adversely affected.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, 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. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, 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 or our licensor were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we or our licensor were the first to file for patent protection of such inventions.

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. The field of gene editing has been the subject of extensive patenting activity and litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain and we may become involved in complex and costly litigation. Our pending and future patent applications may not result in patents being issued which protect our gene editing platform technology and our product candidates or which effectively prevent others from commercializing competitive technologies and product candidates.

No consistent policy regarding the scope of claims allowable in the field of gene editing has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. 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, enforce and defend our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patent rights. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensor are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will be valid and enforceable and provide sufficient protection from competitors.

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 own currently or in the future 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 own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. 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.

In addition, 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. Moreover, some of our owned and in-licensed patents and patent applications may in the future be, co-owned by us with third parties. If we are unable to obtain an exclusive license to such third-partyco-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 may need the cooperation of any such co-owners of our patent rights in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

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

We depend on intellectual property licensed from third parties, and our licensor may not always act in our best interest. If we fail to comply with our obligations under our intellectual property licenses, if the licenses are terminated, or if disputes regarding these licenses arise, we could lose significant rights that are important to our business.

We have licensed and are dependent on certain patent rights and proprietary technology from third parties that are important or necessary to the development of our gene editing technology and product candidates. For example, we are a party to a license agreement with Stanford University pursuant to which we in-license key patent applications for our gene editing platform technology and product candidates (the Stanford License Agreement). This license agreement imposes various diligence, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, our licensor may have the right to terminate our license, in which event we would not be able to develop or market our gene editing platform or any other technology or product candidates covered by the intellectual property licensed under this agreement. For example, under the Stanford License Agreement, we are required to initiate clinical trial programs in accordance with the development plan and development milestones for the development of a licensed product covered by the licensed patent rights. If we fail to initiate such clinical trial programs, our rights with respect to the licensed patent rights may terminate. For more information regarding this agreement, please see the section titled "Business—Our Material Agreements."

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 gene editing platform technology and product candidates in the future. Some licenses granted to us are expressly subject to certain preexisting rights held by the licensor or certain third parties. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in certain territories or fields. For example, the Stanford License Agreement provides that our field of use is solely for the development of prophylactics and therapeutics for sickle cell disease, XSCID, and beta-thalassemia. If we determine that rights to such additional fields are necessary to commercialize our product candidates or maintain our competitive advantage, we may will need to obtain a license from Stanford and/or other third parties in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business.

We do not have complete control in the preparation, filing, prosecution, and maintenance of the patent applications covering the technology that we license from third parties. For example, pursuant to our intellectual property license with Stanford University, our licensor retains control of preparation, filing, prosecution, and maintenance of their patent applications. We cannot be certain that these patent applications will be prepared, filed, prosecuted, maintained, and defended in a manner consistent with the best interests of our business. If our licensor fails to prosecute, and maintain such patent applications, or lose rights to those patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products.

Our licensor has also relied on third-party collaborators or on funds from third parties such that our licensor is not the sole and exclusive owner of the patent rights we have in-licensed. For example, our in-licensed patent rights from the Stanford License are jointly owned by Stanford University and a third party. If third parties have ownership rights to our in-licensed patent rights and we are unable to secure licenses to the rights of such third parties, the license granted to us in jurisdictions where the consent of a co-owner is necessary to grant such a license may not be valid and suchco-owners may be able to license such patent rights to our competitors, and our competitors could market competing products and technology. In addition, our rights to our in-licensed patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of suchin-licensed 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. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, inventions contained within some of ourin-licensed patent applications were made using U.S. government funding. We rely on our licensor to ensure compliance with applicable obligations arising from such

funding, such as timely reporting, an obligation associated with our in-licensed patents and patent applications. The failure of our licensor to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents. For example, the U.S. government could have certain rights in such in-licensed patent applications, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may also exercise its march-in rights if it determines that action is necessary because we or our licensor failed to achieve practical application of the U.S. 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 in-licensed U.S. government-funded inventions may be subject to certain requirements to manufacture product candidates embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations, and prospects significantly.

In the event that our third-party licensor determines that, in spite of our efforts, we have materially breached a license agreement or have failed to meet certain obligations thereunder, it may elect to terminate the license agreement or, in some cases, one or more license(s) under the applicable license agreement and such termination would result in us no longer having the ability to develop and commercialize product candidates and technology covered by that license agreement. In the event of such termination of a third-party in-license, or if the underlying patent rights under a third-party in-license fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our owned and in-licensed patent applications may not provide sufficient protection of our gene editing platform technologies, our product candidates and our future product candidates or result in any competitive advantage.

We own and have in-licensed a number of patent applications that cover gene editing and gene targeting technologies. We have applied for provisional patent applications intended to specifically cover our gene editing platform technology and uses with respect to treatment of particular diseases and conditions, but do not currently own any issued U.S. patents. Each U.S. provisional patent application is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the intentions disclosed in the associated provisional patent applications. We cannot be certain that any of these patent applications will issue as patents, and if they do, that such patents will cover or adequately protect our gene editing platform technologies or our product candidates, or that such patents will not be challenged, narrowed, circumvented, invalidated or held unenforceable. Any failure to obtain or maintain patent protection with respect to our gene editing platform technology and product candidates could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our owned and in-licensed patent applications contain claims directed to compositions of matter on our gene editing product candidates, as well as methods directed to the use of such product candidates for gene therapy treatment. Method-of-use patents do not prevent a competitor or other third party from developing or marketing an identical product for an indication that is outside the scope of the patented method. Moreover, with respect to method-of-use patents, even if competitors or other third parties do not actively promote their product for our targeted indications or uses for which we may obtain patents, providers may recommend that patients use these products off-label, or patients may do so themselves.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued

patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. For example, while our patent applications are pending, we may be subject to a third party pre-issuance submission of prior art to the United States Patent and Trademark Office (USPTO), or become involved in interference or derivation proceedings, or equivalent proceedings in foreign jurisdictions. Even if patents do successfully issue, third parties may challenge their inventorship, validity, enforceability or scope, including through opposition, revocation, reexamination, post-grant and *inter partes* review proceedings. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned or in-licensed patent rights, allow third parties to commercialize our technology or product candidates 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. Moreover, we, or our licensor, 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 our or our licensor's priority of invention or other features of patentability with respect to our owned or in-licensed patent applications. 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. Furthermore, even if they are unchallenged, our patent rights may not adequately protect our intellectual property or prevent others from designing around our platform technology or product candidates. If the breadth or strength of protection provided by the patent applications we own or in-license with respect to our gene editing platform technology and product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in development, testing, and regulatory review of new product candidates, the period of time during which we could market our product candidates under patent protection would be reduced.

Given that patent applications in the United States and other countries are confidential for a period of time after filing, at any moment in time, we cannot be certain that we or our licensor were in the past or will be in the future the first to file any patent application related to our gene editing technology or product candidates. In addition, some patent applications in the United States may be maintained in secrecy until the patents are issued. As a result, there may be prior art of which we or our licensor are not aware that may affect the validity or enforceability of a patent claim, and we or our licensor may be subject to priority disputes. For our in-licensed patent portfolios, we rely on our licensor to determine inventorship, and obtain and file inventor assignments of priority applications before their conversion as PCT applications. A failure to do so in a timely fashion may give rise to a challenge to entitlement of priority for foreign applications nationalized from such PCT applications. We or our licensor may in the future become a party to proceedings or priority disputes in Europe or other foreign jurisdictions. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business.

We may be required to disclaim part or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we or our licensor are aware, but which we or our licensor do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that, if challenged, our patent applications, if issued, would be declared by a court, patent office or other governmental authority to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patent rights. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, that block our efforts or potentially result in our product candidates or our activities infringing such claims. It is possible that our competitors may have filed, and may in the future file, patent applications covering our products or gene editing technology similar to ours. Those patent applications may have priority over our owned patent applications and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. The possibility also exists

that others will develop products that have the same effect as our product candidates on an independent basis that do not infringe our patents or other intellectual property rights, or will design around the claims of our patent applications or our in-licensed patents or patent applications that cover our product candidates.

Likewise, our currently owned patent applications, if issued as patents, and in-licensed patents and patent applications, if issued as patents, directed to our proprietary gene editing technologies and our product candidates are expected to expire from 2036 through 2042, without taking into account any possible patent term adjustments or extensions. Our owned or in-licensed patent applications, if issued as patents, may expire before, or soon after, our first product candidate achieves marketing approval in the United States or foreign jurisdictions. Additionally, no assurance can be given that the USPTO or relevant foreign patent offices will grant any of the pending patent applications we own or in-license currently or in the future. Upon the expiration of our current in-licensed patent applications, if issued as patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patent rights could also have a similar material adverse effect on our business, financial condition, results of operations and prospects

Our owned patent applications and in-licensed patents and patent applications and other intellectual property may be subject to inventorship or ownership disputes and similar proceedings. If we or our licensor are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of our product candidates, which could have a material adverse impact on our business.

We or our licensor may also be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in-licensed patent applications or other intellectual property as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents that issue from such patent applications against third parties, and such cooperation may not be provided to us.

If we or our licensor are unsuccessful in any inventorship or ownership disputes to which we or they are subject, we may lose valuable intellectual property rights through the loss of part or all of our owned, licensed, or optioned patent rights, or such patent claims may be narrowed, invalidated, or held unenforceable, or through loss of exclusive ownership of or the exclusive right to use our owned or in-licensed patent rights. In the event of loss of patent rights as a result of any of these disputes, we may be required to obtain and maintain licenses from third parties, including parties involved in any such inventorship or ownership disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of our product candidates. The loss of exclusivity or the narrowing of our patent rights could limit our ability to stop others from using or commercializing similar or identical technology and product candidates. Even if we or our licensor are successful in an inventorship or ownership dispute, it could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects.

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

We may have limited intellectual property rights outside the United States. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of foreign countries do not protect intellectual property rights to the same extent as federal and state laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. 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 their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of 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 and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our patents and intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Moreover, the initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. 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.

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 our licensor 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.

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

We have entered into a license agreement with a third-party and may need to obtain additional licenses from our existing licensor and others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In either event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including gene editing technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In our license agreement, we are generally responsible for bringing any actions against any third party for infringing on the patent rights we have licensed. Certain of our license agreement, also requires us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In spite of our efforts, our licensor might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby

removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patent rights fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of or gene editing platform technology or product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects. 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 rights to third parties under our collaborative development relationships;
- our diligence obligations under the license agreement with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates 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 licensor and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreement under which we currently license intellectual property or technology from our licensor are complex, and certain provisions in such agreement 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 broaden what we believe to be the scope of the licensor's rights to our intellectual property and technology, or increase what we believe to be our financial or other obligations under the relevant agreement, any 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. As a result, any termination of or disputes over our intellectual property license could result in the loss of our ability to develop and commercialize our gene editing platform or other product candidates or we could lose other significant rights, any of which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. It is also possible that a third party could be granted limited licenses to some of the same technology, in certain circumstances.

We may not be successful in acquiring orin-licensing necessary rights to key technologies or any product candidates we may develop.

We currently have rights to intellectual property, through a license from a third party, to identify and develop product candidates, and we expect to seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Although we have succeeded in licensing technologies from a third-party licensor, Stanford University, in the past, we cannot assure you that we will be able to in-license or acquire additional rights to any product candidates or technologies from Stanford University or other third parties on acceptable terms or at all. For example, there are third parties who possess technologies related to gene editing or other technologies which we may need to in-license.

For example, our agreement with Stanford University provides that our field of use is solely for the development of prophylactics and therapeutics for sickle cell disease, XSCID, and beta-thalassemia. If we determine that rights outside such field are necessary to commercialize our drug candidates or maintain our competitive advantage, we may need to obtain an additional license from Stanford University in order to

continue developing, manufacturing or marketing our drug candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our drug candidates or allow our competitors or others the chance to access technology that is important to our business. For more information regarding these agreements, please see the section titled "Business—Our Material Agreements."

Furthermore, there has been extensive patenting activity in the field of gene editing, and pharmaceutical companies, biotechnology companies, and academic institutions are competing with us or are expected to compete with us in the in the field of gene editing technology and filing patent applications potentially relevant to our business and we are aware of certain third-party patent applications that, if issued, may allow the third party to circumvent our patent rights. For example, we are aware of several third-party patents, and patent applications, that if issued, may be construed to be relevant to our gene editing technology and product candidates. In order to market our product candidates, we may find it necessary or prudent to obtain licenses from such third-party intellectual property holders. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and gene editing technology. We may also require licenses from third parties for certain additional technologies, including technologies relating to gene editing such as high-fidelity nucleases, guide RNA modification and target sequences, as well as technologies for cell manufacturing that we are evaluating for use with our product candidates. In addition, some of our in-licensed patent applications are co-owned with third parties. With respect to any patents co-owned with third parties, we may require licenses to such co-owners' interest to such patents. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such 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 may need the cooperation of any such co-owners of our patent applications in order to enforce such patent rights against third parties, and such cooperation may not be provided to us.

Additionally, we may collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing 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. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

The intellectual property landscape around the technologies we use or plan to use, including gene 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 may prevent, delay or otherwise interfere with our product discovery and development efforts.

Because of the large number of patents issued and patent applications filed in our field, third parties may allege they have patent rights encompassing our product candidates, technologies or methods. Third parties may

assert that we are employing their proprietary technology without authorization and may file patent infringement claims or lawsuits against us, and if we are found to infringe such third-party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. In addition, we have in the past, and may in the future, receive an offer for license from third parties regarding their proprietary intellectual property for which they may believe encompass our product candidates and technologies. We will evaluate such offers for relevance to our business.

The field of gene editing is still in its infancy, and no such therapeutic product candidates have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is evolving and 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.

Our commercial success depends upon our ability and the ability of our collaborators and present and future licensors to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our gene editing platform technology and our product candidates, 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. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our gene editing platform technology and product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. There may also be third-party patents of which we are currently unaware with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. Our product candidates make use of CRISPR-based technology, which is a field that is highly active for patent filings. As of June 2019, it was reported that approximately 2072 patent families worldwide related to CRISPR gene editing inventions and uses as the description and/or claims of these patent families specifically focus on a CRISPR-type system. The extensive patent filings related to CRISPR make it difficult for us to assess the full extent of relevant patents and pending applications that may cover our gene editing platform technology and product candidates and their use or manufacture. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our gene editing platform technology and product candidates. For example, we are aware of a patent portfolio that is co-owned by the University of California, University of Vienna and Emmanuelle Charpentier, or the University of California Portfolio, which contains multiple patents and pending applications directed to gene editing. We are also aware of patents and patent applications directed

to gene editing owned or co-owned by the Broad Institute, MIT and Harvard University, Toolgen, and Sigma Aldrich. Our ability to commercialize our product candidates may be adversely affected if we do not obtain a license to these patents. 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 nonexclusive, 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. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our gene editing platform technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Our ability to commercialize our product candidates in the United States and abroad may be adversely affected if we cannot obtain a license on commercially reasonable terms to relevant third-party patents that cover our product candidates or gene editing platform technology. 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 our product candidates and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third-party's 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 our product candidates 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. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our gene editing platform technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. 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 significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our

competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants 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 our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

We may become involved in lawsuits to protect or enforce our future patents or the patents of our licensor, which could be expensive, time consuming, and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our future patents or the patents of our licensor, or we may be required to defend against claims of infringement. In addition, our future patents or the patents of our licensor also are, and may in the future become, involved in inventorship, priority, validity or enforceability disputes. Countering or defending against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, 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. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent 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, our licensor, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our technology and/or product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). We are currently challenging, and in the future may choose to challenge, third-party patents in patent opposition proceedings in the EPO or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to

obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates, gene editing platform technology or other or proprietary technologies.

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. 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. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government 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 are due to be paid to the USPTO and foreign patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensor to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and foreign patent agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensor to take the necessary action to comply with these requirements with respect to our licensed intellectual property. While 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 a partial or complete loss of patent rights in the relevant jurisdiction. Were a noncompliance event to occur, our competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our gene editing platform technology and product candidates.

As is the case with other biotech and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve 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 could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act (America Invents Act), the United States transitioned from a “first to invent” to a “first-to-file” patent system. Under a “first-to-file” system, assuming that other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on an invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such

third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensor were the first to either file any patent application related to our technology or product candidates or invent any of the inventions claimed in our or our licensor's patents or patent applications. The America Invents Act also includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted, allowing third party submission of prior art and establish a new post-grant review system including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. However, 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.

In addition, 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. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.,* the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. We cannot predict how this and future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Patents have a limited lifespan. The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions including PTE and PTA, may be available, but the life of a patent, and the protection it affords, is limited. For more information regarding PTA and PTE, please see the section titled "Business—Intellectual Property". 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 our product candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain PTE and data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited PTE under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). The Hatch-Waxman Amendments PTE term of up to five years as compensation for patent term lost during the FDA regulatory review process. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent per product 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, even if we were to seek a PTE, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain PTE 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.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our technology and product candidates, we also rely onknow-how and trade secret protection, as well as confidentiality agreements, non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed by or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In the case of consultants and other third parties, the agreements provide that all inventions conceived in connection with the services provided are our exclusive property. However, 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. Additionally, 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. 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.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition,

trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, some courts inside and outside the United States are sometimes less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and growth 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:

- our product candidates will eventually become commercially available in generic or biosimilar product forms;
- others may be able to make gene therapy products that are similar to our product candidates or utilize similar gene editing technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, our licensor, or our current or future collaborators, might not have been the first to make the inventions covered by the pending patent application that we license or may own in the future;
- we, our licensor, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- we, our licensor, or our current or future collaborators, may fail to meet our obligations to the U.S. government regarding any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;
- 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, owned or licensed patent applications or those that we may own in the future will not lead to issued patents;

- it is possible that there are prior public disclosures that could invalidate our owned orin-licensed patent rights, or parts of our owned or in-licensed patent rights;
- it is possible that there are unpublished patent applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- it is possible that our owned or in-licensed patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- issued patents that we obtain in the future may be held invalid, unenforceable, or narrowed in scope, including as a result of legal challenges by our competitors;
- the claims of our owned or in-licensed issued patent applications, if and when issued, may not cover our product candidates;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of license partners or current or future collaborators to the same extent as the laws of the United States;
- the inventors of our owned or in-licensed patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- 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 have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents;
- we may not develop additional proprietary technologies that are patentable;
- any product candidates we develop may be covered by third-parties' patents or other exclusive rights;
- the patents of others may harm our business; or
- we may choose not to file a patent in order to maintain certain trade secrets orknow-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Regulatory and Other Legal Compliance Matters

Because gene editing is novel and the regulatory landscape that will govern our product candidates is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for our product candidates.

The regulatory requirements that will govern any novel gene editing product candidates we develop may continue to evolve. Within the broader genetic medicine field, a limited number of gene therapy products have received marketing authorization from the FDA and the EMA to date. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. 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 (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 (IBC), a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies, such as an IBC, 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 EU. The EMA's Committee for Advanced Therapies (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 Committee for Medicinal Products for Human Use (CHMP), before CHMP adopts its final opinion. In the European Union, the development and evaluation of a gene therapy medicinal products 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 our product candidates, but that remains uncertain at this point.

Adverse developments in post-marketing experience or in clinical trials conducted by others 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 development or approval of our product candidates or limit the use of products utilizing gene 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 novel product candidates such as our product candidates can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene 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 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, require us to perform additional studies or 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.

Because we are developing product candidates in the field of gene editing, in which there is limited clinical experience, there is increased risk that the FDA, the EMA, or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA, or other regulatory authorities will be able to determine the clinical efficacy and safety profile of our product candidates. 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 have developed

or plan to develop product candidates because many of these diseases, including SCD, XSCID and Gaucher disease, 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 thenon-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 may make similar comments with respect to these endpoints and data. Our product candidates 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 gene editing therapeutic product has been approved in the United States or in Europe.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. If clinical trials of any of our current or future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

We have not initiated any clinical trials to date for our IND application for GPH101 in sickle cell disease, and all of our other programs are in discovery or preclinical development. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of the product in humans. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of clinical trials. Interim results of a clinical trial do not necessarily predict final results. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

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.

We may experience numerous unforeseen events during, or as a result of, clinical trials that we conduct, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- challenges in obtaining regulatory clearance or approval to commence clinical trials in the United States from the FDA through an IND, or from other comparable regulatory agencies outside the United States through corresponding applications because these agencies have very limited or no experience with the clinical development of gene editing therapeutics, which may require additional significant testing or data compared to more traditional therapies;
- successfully developing processes for the safe administration of these products, including long-termfollow-up for patients who receive treatment with any of our product candidates;
- delays in reaching a consensus with regulators on trial design and product release specifications;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective CROs, and clinical trial sites;
- clinical trials of our product candidates may fail to show safety or efficacy, or could produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or abandon product development or research programs;
- 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;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment of suitable participants in these clinical trials, which may be particularly challenging for some of the rare genetically defined diseases we are targeting in our most advanced programs, may be delayed or slower than we anticipate; or patients may drop out of these clinical trials at a higher rate than we anticipate;
- we will need to educate medical personnel, including clinical investigators, and patients regarding the potential benefits and side effect profile of each of our product candidates;
- regulatory agencies may require us to perform more extensive or lengthier clinical testing or generate more data, such as long-term toxicology studies, compared to existing therapeutic modalities, or may impose other requirements before permitting us to initiate or rely on a clinical trial;
- 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, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- regulators, IRBs, or independent ethics committees may require that we or our investigators suspend or terminate clinical research or clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- 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, including as a result of delays in the testing, validation, manufacturing, and delivery of our product candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- we may face challenges in sourcing clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates, which may include importing or exporting materials between different jurisdictions;
- we may be unable to develop a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment; and
- we may face challenges in establishing sales and marketing capabilities in anticipation of, and after obtaining, any regulatory approval to gain market authorization.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted or the relevant ethics committee, the Data Safety Monitoring Board (DSMB), for such trial, or the FDA or other relevant regulatory authorities. We or such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, resulting in the imposition of a clinical hold, manufacturing or quality control issues, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

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 or other testing of our product candidates, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our such product candidates or not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, 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 regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a REMS or through modification to an existing REMS;
- be sued; or
- experience damage to our reputation.

Product development costs will also increase if we or our collaborators experience delays in clinical trials or other testing or in obtaining 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 our product candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our product candidates, any of which may harm our business, financial condition, results of operations, and prospects.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell our product candidates in the European Union and other foreign jurisdictions, we or our third-party collaborators must obtain separate marketing approvals (a single one for the European Union) and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product candidate be approved for reimbursement before the product candidate can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in any jurisdiction, which would materially impair our ability to generate revenue.

On June 23, 2016, the UK electorate voted in favor of leaving the EU, commonly referred to as “Brexit.” Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty and the withdrawal of the United Kingdom from the EU formally took effect on January 31, 2020 under the terms of the Withdrawal Agreement. Following the United Kingdom’s departure from the EU, there was a “transition period” during which the United Kingdom was essentially treated as a Member State of the EU and the regulatory regime remained the same across the United Kingdom and the

EU, while the future relationship between the United Kingdom and the EU was formally negotiated. This transition period ended on December 31, 2020. The United Kingdom and the EU have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and will become formally applicable once ratified by both the United Kingdom and the EU. This agreement provides details on how some aspects of the UK and EU's relationship will operate going forwards however there are still many uncertainties.

Since the regulatory framework for pharmaceutical products in the United Kingdom relating to quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit will materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom, now that the United Kingdom legislation may diverge from EU legislation. For example, now the transition period has expired, Great Britain will no longer be covered by the centralized procedure for obtaining EEA-wide marketing authorization from the EMA and a separate process for authorization of drug products will be required in Great Britain resulting in an authorization covering the United Kingdom or Great Britain only. For a period of two years from January 1, 2021, the MHRA may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a UK marketing authorization. A separate application will, however, still be required. Longer term, the United Kingdom is likely to develop its own legislation that diverges from that in the EU.

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

The FDA, the EMA, and other regulatory agencies closely regulate the post-approval marketing and promotion of product candidates to ensure that they are marketed only for the approved indications and in

accordance with the provisions of the approved labeling. The FDA, the EMA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we market our product candidates foroff-label use, we may be subject to enforcement action foroff-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act (FDCA), and other statutes, including the False Claims Act (FCA), and equivalent legislation in other countries relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state and other countries' health care fraud and abuse laws and state consumer protection laws. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

In addition, later discovery of previously unknown problems with our products, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various negative consequences, including:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a therapy;
- restrictions on the distribution or use of a therapy;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution, or disgorgement of profits or revenue;
- restrictions on future procurements with governmental authorities;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations, and prospects.

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

Healthcare providers, including physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we may develop for which we obtain marketing approval. Our current and future arrangements with third-party payors, healthcare providers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the

business or financial arrangements and relationships through which we market, sell, and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, including certain laws and regulations applicable only if we have marketed products, include the following:

- the civil FCA, prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the FCA 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 FCA can result in very significant monetary penalties, for each false claim and treble the amount of the government's damages. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;
- the federal Anti-Kickback Statute prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. 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. A violation of the federal Anti-Kickback Statute can also form the basis for FCA liability;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the 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 (HITECH), and its implementing regulations, including the final omnibus rule published on January 25, 2013, imposes, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain, transmit, or obtain, protected health information in connection with providing a service for or on behalf of a covered entity, and their covered subcontractors. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions;
- the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products foroff-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- federal transparency laws, including the federal Physician Payment Sunshine Act created under the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), and its implementing regulations, which requires manufacturers of certain drugs, devices, medical supplies, and biologics, among others, to track and disclose payments under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) and other transfers of value they make to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and

investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. This information is subsequently made publicly available in a searchable format on a Centers for Medicare & Medicaid Services (CMS), website. Failure to disclose required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and/or other healthcare providers; and

- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws also require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments to health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to significant penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, individual imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

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. The provision of benefits or advantages to also induce or reward improper performance generally is governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the United Kingdom. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the EU.

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

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

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

Within the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the ACA and the ongoing efforts to modify or repeal that legislation. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Other aspects of healthcare reform, such as expanded government enforcement authority and heightened standards that could increase compliance-related costs, could also affect our business. Modifications have been implemented under the previous presidential administration and additional modifications or repeal may occur.

There have been executive, judicial and congressional challenges to certain aspects of the ACA. For example, the U.S. Supreme Court is currently reviewing the constitutionality of the ACA, but it is unknown when a decision will be reached. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. Although the Supreme Court has not yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results, and we cannot predict how future federal or state legislative, judicial or administrative changes relating to healthcare reform will affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction, asked 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 up to 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester reductions from May 1, 2020 through December 31, 2021. On January 2, 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, 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. The Bipartisan Budget Act (BBA), also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Furthermore, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS, issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. At the state level, legislatures have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Fast track, breakthrough, or regenerative medicine advanced therapy designation by the FDA may not actually lead to a faster development or regulatory review or approval process, and does not assure FDA approval of our product candidates.

FDA's fast track, breakthrough, and regenerative medicine advanced therapy (RMAT), programs are intended to expedite the development of certain qualifying products intended for the treatment of serious diseases and conditions. If a product candidate is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the product's potential to address an unmet medical need for this condition, the sponsor may apply for FDA fast track designation. A product candidate may be designated as a

breakthrough therapy if it is intended to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A product candidate may receive RMAT designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening condition, and preliminary clinical evidence indicates that the product candidate has the potential to address an unmet medical need for such condition. While we may seek fast track, breakthrough, and/or RMAT designation, there is no guarantee that we will be successful in obtaining any such designation. Even if we do obtain such designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. A fast track, breakthrough, or RMAT designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. In addition, the FDA may withdraw fast track, breakthrough, or RMAT designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track, breakthrough, and/or RMAT designation alone do not guarantee qualification for the FDA's priority review procedures.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidates.

If the FDA determines that a product candidate is intended to treat a serious disease or condition and, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, prevention, or diagnosis of such disease or condition, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review a marketing application is six months from filing of the application, rather than the standard review period of ten months. We may request priority review for certain of our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may disagree and decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan product candidates by the EMA in the European Union. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for another similar product candidate for the same orphan therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate

for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

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

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the EMA, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the EMA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Upon the effectiveness of this registration statement, we will adopt a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

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 Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended (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 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.

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

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

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. Additionally, as of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to theCOVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. Since March 2020, foreign and domestic inspections by the FDA have largely been on hold with the FDA announcing plans in July 2020 to resume prioritized domestic inspections. However, the FDA's inspection activities will depend on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future shutdowns of other government agencies, such as the SEC, may also impact our business through review of our public filings and our ability to access the public markets.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies and contractual obligations could adversely affect our business.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States and EU. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws, regulations, contractual obligations, or standards could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, customers, or business partners, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to the HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation.

If we are unable to properly protect the privacy and security of protected health information, we could be alleged or actually found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. The U.S. Department of Health and Human Services, of HHS, has the discretion to impose penalties without attempting to resolve violations through informal means. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Risks Related to Employee Matters, Managing Growth, Public Health and Information Technology

Our future success depends on our ability to retain our Chief Executive Officer, Chief Operating Officer, Chief Business Officer and other key executives and employees and to attract, retain, and motivate qualified personnel.

We are highly dependent on Josh Lehrer, M.D., our Chief Executive Officer, Ms. Katherine Vega Stultz, our Chief Operating Officer and Mr. Philip P. Gutry, our Chief Business Officer, Head of Finance & Investor Relations, as well as the other principal members of our management and scientific teams. Dr. Lehrer, Ms. Stultz and Mr. Gutry and such other principal members are employed “at will,” meaning we or they may terminate the employment 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.

Recruiting and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel is critical to our success. We may not be able to attract and retain these 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 and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The inability to recruit, or loss of services of certain executives, key employees, consultants, or advisors, may impede the progress of our research, development, and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations, and prospects.

We expect to expand our research and development, clinical and regulatory, and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As December 31, 2020, we had 21 full-time employees, and, in connection with the advancement of our development programs and becoming a public company, we expect to increase the number of our employees and the scope of our operations further, particularly in the areas of research and clinical development, regulatory affairs, and sales and marketing. To manage our anticipated future growth, 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 expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

As a growing biotechnology company, we are actively developing our platform technology and pursuing new product candidates in multiple therapeutic areas. Successfully developing product candidates for and fully understanding the regulatory and manufacturing pathways to all of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize our product candidates, if approved, will depend in part on our ability to effectively manage the future development and expansion of our Company.

Our internal computer systems, or those of our third-party vendors, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

Our internal computer systems and those of our current and any future third-party vendors, collaborators and other contractors or consultants are vulnerable to damage or interruption from computer viruses, malware (including ransomware), phishing attacks, computer hackers, malicious code, employee theft or misuse, intentional or accidental action or lack of action by our employees or any contractors with access to our systems that leads to the introduction of vulnerabilities, denial-of-service attacks, sophisticated nation-state and nation-

state-supported actors, supply chain attacks, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we seek to protect our information technology systems from system failure, accident and security breach, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets, personal information, or other proprietary information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counter-parties and data subjects could be material. In addition, our remediation efforts may not be successful. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our third-party vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential, personal or proprietary information, we could incur liability including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

Risks Related to This Offering and Ownership of Our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. Although we expect to list our common stock on the Nasdaq Global Market, an active trading market for our common stock may never develop or be sustained following this offering. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $ per share, representing the difference between the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and our pro forma net tangible book value per share after giving effect to this offering and the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering. Moreover, we issued options in the past that allow the holders to acquire common stock at prices significantly below the assumed initial public offering price. As of , 2021, there were shares subject to outstanding options with a weighted-average exercise price of $ per share. To the extent that these outstanding options are ultimately exercised or the underwriters exercise their over-allotment option, you will incur further dilution. For a further description of the dilution you will experience immediately after this offering, see the section titled "Dilution."

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock was determined through negotiations with the underwriters. This initial public offering price may vary from the market price of our common stock after the

offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by those factors discussed in this "Risk Factors" section and many others, including:

- the success of existing or new competitive product candidates or technologies;
- the timing and results of preclinical studies and clinical trials for our product candidates;
- failure or discontinuation of any of our product development and research programs;
- 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;
- developments or changing views regarding the use of genetic medicines, including those that involve gene editing;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts, if any, that cover our stock;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- the COVID-19 pandemic, natural disasters, or major catastrophic events;
- general economic, industry, and market conditions; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future.

Securities litigation could result in substantial costs and divert management's attention and resources from our business.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. After this offering and after giving effect to the conversion of all outstanding shares of our preferred stock into shares of our common stock upon the closing of this offering, we will have shares of common stock outstanding, or shares if underwriters exercise their over-allotment option in full, in each case based on the 24,998,807 shares of our common stock outstanding as of December 31, 2020. Of these shares, the shares (or shares if the underwriters exercise their option to purchase additional shares in full) we are selling in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining shares are currently restricted under securities laws or as a result of lock-up or other agreements, but will be able to be sold after this offering as described in the "Shares eligible for future sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of shares of our common stock will have rights, subject to 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. We also plan to register all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus. 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.

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

Prior to this offering, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately % of our voting stock and, upon the closing of this offering, that same group will beneficially own approximately % of our outstanding voting stock (based on the number of shares of common stock outstanding as of December 31, 2020, assuming no exercise of the underwriters' over-allotment option, no exercise of outstanding options and no purchases of shares in this offering by any of this group), in each case assuming the conversion of all outstanding shares of our redeemable convertible preferred stock into shares of our common stock immediately prior to the closing of this offering. After this offering, this group of stockholders will have the ability to control us through this ownership position even if they do not purchase any additional shares in this offering. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

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

We are an "emerging growth company," as defined in the JOBS Act and may remain an emerging growth company for up to five years. 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. These exemptions include not being required to comply with the auditor

attestation requirements of Section 404 of SOX, 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 stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," meaning that the market value of our stock held bynon-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than $700 million and our annual revenue is less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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 more volatile.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in the section titled "Use of Proceeds." Accordingly, you will have to rely upon the judgment of our management with respect to the use of the proceeds, with only limited information concerning management's specific intentions. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. 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. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Provisions in our amended and restated certificate of incorporation, our amended andrestated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management, which could depress the trading price of our common stock.

Our amended and restated certificate of incorporation, amended andrestated by-laws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation and by-laws, which will become effective upon the closing of this offering, 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 make, alter, amend or repeal our amended and restatedby-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.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. 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 we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware (DGCL), 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.

Any provision of our amended and restated certificate of incorporation, amended andrestated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated by-laws will designate the Court of Chancery of the State of Delaware as the exclusive forum for certain state law litigation that may be initiated by our stockholders, which could limit our stockholders' ability to litigate disputes with us in a different judicial forum.

Pursuant to our amended and restated by-laws, as will be in effect upon the completion of this offering, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware, our amended and restated certificate of incorporation or our amended and restated by-laws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or by-laws; or (v) any action asserting a claim governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. This exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Unless we consent in writing to the selection of an alternate forum, the United States federal district courts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. The forum selection clause in our amended and restated by-laws may limit our stockholders' ability to litigate disputes with us in a different judicial forum.

Our operations are vulnerable to interruption by fire, earthquakes, power loss, telecommunications failure, terrorist activity, pandemics and other events beyond our control, which could harm our business.

Our facilities are located in California. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, fire, earthquake, power loss, terrorist activity, pandemics or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

General Risk Factors

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

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

If we fail to establish and maintain proper and effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could decline significantly.

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. As a public company, we will be required to maintain internal controls over financial reporting and to report any material weaknesses in such internal controls. Section 404 of SOX requires annual management assessment of the effectiveness of our internal control over financial reporting. However, our auditors will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of SOX until we are no longer an emerging growth company if we continue to take advantage of the exemptions available to us through the JOBS Act.

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 could cause investors to lose confidence in the accuracy and completeness of our financial reports and could cause the market price of our common stock to decline significantly.

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

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting, and other expenses that we did not incur as a private company. SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select 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 becoming, and our efforts 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. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of SOX, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. 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 Section 404 of SOX 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 that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that 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 Section 404 of SOX. 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.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon the closing of this offering, we will become subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Unfavorable global economic conditions could adversely affect our business, financial condition, results of operations or prospects.

Our business, financial condition, results of operations or prospects could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our product candidates, if approved, or our inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections titled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials of our lead product candidates, GPH101, GPH201 and GPH301, including the initiation and progress of, and results from, our planned Phase 1/2 clinical trial of GPH101 and whether the clinical trial will support the intended uses for treatment of sickle cell disease, and future clinical trials or these and any of our other product candidates;
- the therapeutic potential of our product candidates, and the disease indications for which we intend to develop our product candidates;
- the timing and likelihood of, and our ability to obtain and maintain, regulatory clearance of our IND applications for and regulatory approval of our product candidates;
- our ability and the ability of third-party suppliers upon which we rely to manufacture our product candidates for clinical development and, if approved, for commercialization, and the timing and costs of such manufacture;
- estimates of our expenses, ongoing losses, future revenue, capital requirements and our need for or ability to obtain additional funding before we can expect to generate any revenue from product sales;
- our ability to compete with companies currently marketing or engaged in targeted gene integration therapies;
- our ability to establish or maintain collaborations, partnerships or strategic relationships;
- our ability to create a pipeline of product candidates;
- our ability to advance any product candidate into, and successfully complete clinical trials;
- our ability to obtain and maintain intellectual property protection for our current and future product candidates, the duration of such protection and our ability to operate our business without infringing on the intellectual property rights of others;
- our ability to retain and recruit key personnel;
- our expectations regarding use of the proceeds from this offering;
- our financial performance;
- our competitive position and the development of and projections relating to our competitors or our industry, including in gene editing and gene therapy;
- the impact of the COVID-19 pandemic on our business or operations;
- the impact of laws and regulations in the United States and foreign countries; and

- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled "Risk Factors" and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements.

MARKET AND INDUSTRY DATA

We obtained the market, industry and competitive position data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies and publicly available information in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market and competitive position data included in this prospectus are reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise their over-allotment option to purchase additional shares in full, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Similarly, each increase or decrease of 1.0 million shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease, as applicable, our net proceeds from this offering by approximately $ million, assuming the assumed initial public offering price to the public remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial price to the public or the number of shares by these amounts would have a material effect on the uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

The principal purposes of this offering are to obtain additional capital to support our operations, to create a public market for our common stock and to facilitate our future access to the public equity markets.

We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $ million to fund our development of GPH101 for the treatment of SCD through ;
- approximately $ million to fund our development of GPH201 for the treatment of XSCID through ;
- approximately $ million to fund our development of GPH301 for the treatment of Gaucher disease through ;
- approximately $ million to fund our current discovery programs in CCR5 and alphaglobin through ; and
- the remainder, if any, to fund our other research and development activities, working capital and other general corporate purposes.

We may also use a portion of the net proceeds to acquire or invest in new businesses, partnerships, technology or assets, although we have no present commitments or obligations to do so. We evaluate such opportunities and engage in related discussions with third parties from time to time.

Based on our current operating plan, we believe that our existing cash and cash equivalents, together with the net proceeds from this offering, will be sufficient to fund our operating expenses and meet our working capital and capital expenditure needs at least through . Our expected use of net proceeds from this offering represents our current intentions based upon present plans and business conditions. The net proceeds from this offering, together with our existing cash and cash equivalents, will not be sufficient to fund any of our product candidates through regulatory approval, and we anticipate needing to raise additional capital to complete the development of and commercialize our product candidates.

The expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions. We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering. Due to uncertainties inherent in the product development process, it is difficult to estimate the exact amounts of the net proceeds that will be used for any particular purpose. We may use our existing cash and cash equivalents and the future payments, if any, generated from any future collaboration agreements to fund our operations, either of which may alter the amount of net proceeds used for a particular purpose. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts as well as our interactions with regulatory authorities. Accordingly, we will have broad discretion in using these proceeds.

Pending the uses described above, we plan to invest the net proceeds of this offering in short- and immediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We do not anticipate paying any dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. Any future determination to declare dividends will be subject to the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2020:

- on an actual basis;
- on a pro forma basis to give effect to (i) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock (including shares of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock issued in February 2021 and March 2021, respectively) into an aggregate of 74,812,432 shares of our common stock immediately prior to the closing of this offering, and (ii) the adoption, filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to give effect to (i) the pro forma adjustments described above, and (ii) the issuance and sale of shares of our common stock in this offering at the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions, and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth in the sections titled "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of December 31, 2020		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
		(in thousands, except share and per share data) (unaudited)	(unaudited)
Cash and cash equivalents	$ 19,782	$	$
Redeemable convertible preferred stock, par value $0.00001 per share; 45,024,986 shares authorized, 30,019,945 issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 55,608	$	$
Stockholders' deficit:			
Common stock, par value $0.00001 per share; 80,000,000 shares authorized, 24,998,807 shares issued and outstanding, actual; shares authorized, 99,811,239 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	—		
Preferred stock, $0.00001 par value per share; no shares authorized, issued or outstanding, actual; shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—		
Additional paid-in capital	5,183		
Accumulated deficit	(70,591)		
Total stockholders' deficit	(65,408)		
Total capitalization	$ (9,800)		

(1) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, each of our pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' deficit, and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated

underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million in the number of shares we are offering would increase or decrease, as applicable, each of our pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' deficit, and total capitalization by approximately $ million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of shares of our common stock outstanding on a pro forma and pro forma as adjusted basis in the table above is based on 99,811,239 shares of common stock outstanding as of December 31, 2020, including our (i) our restricted common stock subject to vesting and (ii) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock (including shares of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock issued in February 2021 and March 2021, respectively) into an aggregate of 74,812,432 shares of our common stock immediately prior to the completion of this offering, and excludes:

- 746,000 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2020, with a weighted-average exercise price of $0.12 per share;
- 5,329,944 shares of our common stock issuable upon the exercise of outstanding stock options granted after December 31, 2020, with a weighted-average exercise price of $2.14 per share;
- 5,020,152 shares of our common stock reserved for future issuance under our 2020 Plan, as of December 31, 2020;
- shares of our common stock reserved for future issuance under our 2021 Plan, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 Plan; and
- shares of our common stock reserved for future issuance under our 2021 ESPP, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 ESPP.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book (deficit) value per share of our common stock immediately after this offering.

Our historical net tangible book (deficit) value per share is determined by dividing our total tangible assets less our total liabilities and redeemable convertible preferred stock, which are not included within stockholders' deficit by the number of shares of common stock outstanding. Our historical net tangible book value (deficit) as of December 31, 2020 was $65.4 million, or $2.62 per share.

Our pro forma net tangible book (deficit) value as of December 31, 2020 was $ million, or $ per share. Our pro forma net tangible book (deficit) value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of December 31, 2020, assuming the automatic conversion of all outstanding shares of our redeemable convertible preferred stock (including shares of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock issued in February 2021 and March 2021, respectively) into an aggregate of 74,812,432 shares of common stock, which conversion will occur immediately prior to the completion of this offering.

Our pro forma as adjusted net tangible book (deficit) value represents our pro forma net tangible book (deficit) value, plus the effect of the sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2020 would have been $ million, or $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ per share to purchasers of common stock in this offering, as illustrated in the following table:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of December 31, 2020	$ 2.62	
Pro forma increase in net tangible book value (deficit) per share as of December 31, 2020		
Pro forma net tangible book value per share as of December 31, 2020		
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new investors participating in this offering		$

If the underwriters' over-allotment option is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

Each $1.00 increase or decrease in the assumed public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, our pro forma as adjusted net tangible book value by $ million, or $ per share, and dilution per share to investors in this offering by $ per share, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions, and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Similarly, each increase or decrease of 1.0 million in the number of shares we are offering would increase or decrease, as applicable, our pro forma as adjusted net tangible book value by approximately $ million, or approximately $ per share and would increase or decrease, as applicable, dilution per share to investors in this offering by approximately $ per share, assuming the assumed initial public offering price per share remains the same and after deducting estimated underwriting discounts and commissions, and estimated offering expenses payable by us.

If the underwriters' over-allotment option is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

The following table summarizes, as of December 31, 2020, on a pro forma as adjusted basis (but before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us), the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common stock and redeemable convertible preferred stock, cash received from the exercise of stock options, and the value of any stock issued for services and the weighted-average price paid per share:

	Shares Purchased		Total Consideration		Weighted-Average Price Per Share
	Number	Percent	Amount	Percent	
	(in thousands, except per share amounts and percentages)				
Existing stockholders before this offering		%	$	%	$
New investors participating in this offering					$
Totals		100.0%	$	100.0%	

The foregoing tables and calculations (other than the historical net tangible book value calculations) are based on 99,811,239 shares of our common stock outstanding as of December 31, 2020, including (i) our restricted common stock subject to vesting and (ii) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock (including shares of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock issued in February 2021 and March 2021, respectively) into an aggregate of 74,812,432 shares of our common stock immediately prior to the completion of this offering), and excludes:

- 746,000 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2020, with a weighted-average exercise price of $0.12 per share;
- 5,329,944 shares of our common stock issuable upon the exercise of outstanding stock options granted after December 31, 2020, with a weighted-average exercise price of $2.14 per share;
- 5,020,152 shares of our common stock reserved for future issuance under our 2020 Plan as of December 31, 2020;
- shares of our common stock reserved for future issuance under our 2021 Plan, which will become available for issuance upon the effectiveness of the registration statement of which this

prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 Plan; and

- shares of our common stock reserved for future issuance under our 2021 ESPP, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2021 ESPP.

To the extent that any outstanding options are exercised, new options are issued under our stock-based compensation plans or we issue additional shares of common stock or convertible debt in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED FINANCIAL DATA

The following tables set forth our selected statements of operations and comprehensive loss data for the years ended December 31, 2019 and 2020 and our selected balance sheet data as of December 31, 2019 and 2020, and have been derived from our audited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the following selected financial data together with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus and our financial statements and the related notes included elsewhere in this prospectus. The selected financial data included in this section are not intended to replace the financial statements and the related notes included elsewhere in this prospectus and are qualified in their entirety by our financial statements and the related notes included elsewhere in this prospectus.

	Year Ended December 31,	
	2019	2020
	(in thousands, except share and per share amounts)	
Statements of Operations and Comprehensive Loss Data:		
Operating expenses:		
Research and development	$ —	$ 9,123
General and administrative	29	4,377
Total operating expenses	29	13,500
Loss from operations	(29)	(13,500)
Other income (expense), net:		
Related party convertible note interest expense	(80)	(40)
Change in fair value of the redeemable convertible preferred stock tranche liabilities	—	(54,833)
Total operating income (expense), net	(80)	(54,873)
Net loss and comprehensive loss	$ (109)	$ (68,373)
Net loss per share attributable to common stockholders, basic and diluted(1)	$ (109,000)	$ (12.31)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	1	5,554,899
Pro forma net loss per share attributable to common stockholders, basic and diluted(2)		$ (0.38)
Weighted-average shares outstanding used in computing pro forma net loss per share attributable to common stockholders, basic and diluted(2)		35,574,844

(1) See Notes 2 and 11 to our financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(2) See the section titled "Management's Discussion and Analysis of Financial Conditions and Results of Operations—Unaudited Pro Forma Information" for an explanation of the calculation of our basic and diluted pro forma net loss per share, and the weighted-average number of shares outstanding used in the computation of the per share amounts.

	As of December 31,	
	2019	2020
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 6	$ 19,782
Working capital(1)	(2,218)	(10,945)
Total assets	6	22,564
Redeemable convertible preferred stock	—	55,608
Additional paid-in capital	—	5,183
Accumulated deficit	(2,218)	(70,591)
Total stockholders' deficit	(2,218)	(65,408)

(1) We define working capital deficit as current assets less current liabilities. See our financial statements appearing elsewhere in this prospectus.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our financial statements and related notes and other financial information included elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon our current plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and beliefs. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under the section titled "Risk Factors" and elsewhere in this prospectus. You should carefully read the "Risk Factors" section of this prospectus to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage, next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to potentially cure a wide range of serious and life-threatening diseases. We are pioneering a precision gene editing approach to achieve one of medicine's most elusive goals: to precisely "find & replace" any gene in the genome. Our next-generation gene editing platform allows us to precisely correct mutations, replace entire disease-causing genes with normal genes, or insert new genes into predetermined, safe locations. We believe our approach could enable nearly limitless applications to transform human health, including directly correcting mutations, engineering cells to permanently deliver therapeutic proteins, and precisely engineering effector cells to treat or cure a wide range of serious genetic and other diseases, including cancer, autoimmune and neurodegenerative diseases.

Our lead product candidate GPH101 is a highly differentiated approach with the potential to directly correct the mutation that causes SCD and restore normal HgbA expression. Curing sickle cell disease by correcting the disease-causing point mutation to normal is viewed as the gold-standard for curing SCD and has been the dream of treating physicians for generations. We have received clearance of our IND and we intend to enroll the first patient in a Phase 1/2 clinical trial of GPH101 in . We are also advancing our research programs and pipeline of potentially one-time curative therapies for a wide range of genetic and other serious diseases and intend to file an IND for a second program by .

We were incorporated in Ontario, Canada in June 2017 as Longbow Therapeutics Inc. and were reincorporated in the State of Delaware in October 2019. In February 2020, we changed our name to Integral Medicines, Inc. and in August 2020, we changed our name to Graphite Bio, Inc. Research and development of our initial technology ceased at the end of 2018 and we did not have any significant operations or any research and development activities in 2019. In March 2020, we identified new gene editing technology which we sought to further develop, and we licensed the related intellectual property rights from The Board of Trustees of the Leland Stanford Junior University (Stanford) in December 2020.

Since our inception in June 2017, we have devoted substantially all of our resources to performing research and development, enabling manufacturing activities in support of our product development efforts, hiring personnel, acquiring and developing our technology and product candidates, organizing and staffing our Company, performing business planning, establishing our intellectual property portfolio, raising capital and providing general and administrative support for these activities. We have one product candidate in early clinical development and all of our other product candidates are in preclinical development, and we do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily with an aggregate of $197.7 million in aggregate gross proceeds from the sales of our redeemable convertible preferred stock and the issuance of convertible notes. We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to

finance our cash needs through public or private equity or debt financings, and collaborations, strategic alliances and licensing arrangements with third parties.

We have incurred significant operating losses since inception. As of December 31, 2020, we had cash and cash equivalents of $19.8 million and an accumulated deficit of $70.6 million. We expect to continue to incur substantial losses for the foreseeable future, and our transition to profitability will depend upon successful development, approval and commercialization of our product candidates and upon achievement of sufficient revenues to support our cost structure. We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take at least several years. We may never achieve profitability, and unless and until then, we will need to continue to raise additional capital. Based upon our current operating plan, we estimate that our existing cash and cash equivalents as of the date of this prospectus will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next months.

We expect our expenses will increase substantially in connection with our ongoing and planned activities, as we:

- advance product candidates through preclinical studies and clinical trials;
- manufacture supplies for our preclinical studies and clinical trials;
- acquire, discover, validate and develop additional product candidates and technologies;
- attract, hire and retain additional personnel;
- operate as a public company;
- implement operational, financial and management systems;
- pursue regulatory approval for any product candidates that successfully complete clinical trials;
- expand or establish additional facilities for our growing business and operations;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval and related commercial manufacturing build-out; and
- obtain, maintain, expand and protect our portfolio of intellectual property rights.

We rely and will continue to rely on third parties in the conduct of our preclinical studies and clinical trials and for manufacturing and supply of our product candidates. We have no internal manufacturing capabilities, and we may continue to rely on third parties for our preclinical and clinical trial materials, of which the main suppliers are single-source suppliers. Given our stage of development, we do not yet have a marketing or sales organization or commercial infrastructure. Accordingly, if we obtain regulatory approval for any of our product candidates, we also expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from sales of any product for which we receive regulatory approval, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and may be forced to reduce our operations.

Business Impact of COVID-19 Pandemic

In March 2020, the World Health Organization declared the global novel COVID-19, outbreak a pandemic. The ongoing COVID-19 pandemic may continue to affect our ability to initiate and complete preclinical studies, delay the initiation of our planned clinical trials or future clinical trials or the progress or completion of our ongoing clinical trials, impede regulatory activities, disrupt the supply chain and the manufacture or shipment of

drug substances and finished drug products for our product candidates for use in our clinical trials, impair testing, monitoring, data collection and analysis and other related activities or have other adverse effects on our business, financial condition, results of operations and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations and our ability to raise additional funds to support our operations. For example and in light of the ongoing COVID-19 pandemic, our partner Stanford was delayed in making an IND-filing. In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic, and we may face similar volatility in our stock price.

We are following, and will continue to follow, recommendations from the U.S. Centers for Disease Control and Prevention as well as federal, state, and local governments regarding working-from-home practices for non-essential employees as well as return-to-work policies and procedures. We expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees and other business partners in light of the pandemic.

While our operations to date have not been significantly impacted by the COVID-19 pandemic, we cannot at this time predict the specific extent, duration, or full impact that the COVID-19 pandemic will have on our business, financial condition and operations, including planned clinical trials and clinical development timelines. The impact of the COVID-19 pandemic on our financial performance will depend on future developments, including the duration and spread of the pandemic, its impact on our clinical trial enrollment, trial sites, CROs, CMOs and other third parties with whom we do business, its impact on regulatory authorities and our key scientific and management personnel, progress of vaccination and related governmental advisories and restrictions. These developments and the impact of the COVID-19 pandemic on the financial markets and the overall economy are highly uncertain and cannot be predicted. If the financial markets or the overall economy are impacted for an extended period, our business may be materially adversely affected.

Stanford Exclusive License Agreement

In December 2020, we entered into an exclusive license agreement (the License Agreement), with The Board of Trustees of the Leland Stanford Junior University (Stanford), pursuant to which Stanford granted us a worldwide license to specified technology and patent rights to develop, manufacture and commercialize human prophylactic and therapeutic products. Other than with respect to specified, broadly applicable assays and procedures and subject to retained rights by Stanford, the license is exclusive with respect to human prophylactic and therapeutic products for the treatment of SCD, XSCID and beta thalassemia. The license is non-exclusive with respect to those broadly applicable assays and procedures and with respect to all human prophylactic and therapeutic products other than for the treatment of SCD, XSCID and beta thalassemia. Please see the section titled “Business—Our Material Agreements” for additional information concerning the intellectual property related to the License Agreement.

Pursuant to the License Agreement, we paid an upfront license fee of $50,000, and as additional consideration for the license, we agreed to issue to Stanford approximately 1.6 million shares of our common stock. The acquisition of the exclusive license, including patent rights and know-how, and clinical supplies was accounted for as an asset acquisition and as the acquired technology and inventories did not have an alternative use, the total consideration of $2.8 million was recorded as research and development expense in the statements of operations and comprehensive loss for the year ended December 31, 2020. We are obligated to pay Stanford an annual license maintenance fee on each anniversary of the effective date of the License Agreement. The annual license maintenance fee initially is $5,000 and will increase to $50,000 in three increments over the first seven anniversaries of the effective date of the License Agreement. After the first commercial sale of a product falling within the scope of the license (Licensed Product), the annual license maintenance fee is $200,000.

We are required to share with Stanford a portion of any non-royalty income we receive from sublicensing the licensed patent rights or technology, subject to specified exclusions. With respect to sublicenses granted to

products for the treatment of SCD, XSCID and beta thalassemia, the portion of sublicense income we must share with Stanford varies by indication and declines from between a mid-teens to a second quartile double-digit percentage prior to the filing of an IND to between a high single-digit to very low double-digit percentage upon achievement of a specified clinical milestone. With respect to sublicenses granted under the licensed technology rights and not licensed patent rights, the portion of sublicense income shared with Stanford declines from between a mid single-digit and very low double-digit percentage prior to the filing of an IND to a low single-digit percentage after filing of an IND.

We are obligated to make payments to Stanford with respect to each Licensed Product of up to an aggregate of $13.0 million upon the achievement of certain development, regulatory and commercial milestones. Such amounts are payable only once upon the first occurrence of a particular milestone event with respect to each Licensed Product and only once with respect to each new indication covered by any of the Licensed Products.

We also are obligated to pay Stanford low single-digit royalties based on worldwide annual net sales of any Licensed Product, subject to specified reductions. We will be obligated to continue to pay royalties on a Licensed Product-by-Licensed Product and country-by-country basis, until the latest of (i) the expiration of the last valid claim under the licensed patents that covers the sale or manufacture of such Licensed Product in such country, (ii) the expiration of any period of regulatory exclusivity with respect to such Licensed Product in such country or (iii) the expiration of ten years after the first commercial sale of such Licensed Product in such country.

The term of the License Agreement expires on the later of (i) the expiration of the last patent or abandonment of the last patent application within the license patent rights or (ii) the expiration of all royalty terms with respect to Licensed Products. The License Agreement may be terminated by us at will or by Stanford if we remain in breach of the License Agreement following a cure period to remedy the breach.

We are required to use diligent efforts to manufacture, market and sell Licensed Products for the treatment of each of SCD, XSCID and beta thalassemia. In addition, we are required to achieve specified milestones by specified dates with respect to Licensed Products for the treatment of each of SCD, XSCID and beta thalassemia. If we fail to satisfy our diligence obligations, Stanford may terminate the License Agreement for our breach. For more details on the License Agreement, please see the section titled “Business—Our Material Agreements.”

Components of Results of Operations

For the year ended December 31, 2019, we incurred total expenses of $0.1 million, consisting primarily of professional legal, tax, and accounting fees and recorded a net loss of $0.1 million. Our operating results were immaterial for the year ended December 31, 2019 and, therefore, are omitted from the discussion of results of operations and liquidity below.

Operating Expenses

Research and Development

Research and development costs consist primarily of external and internal costs incurred for our research activities and the development of our gene editing platform and associated rights which we licensed in December 2020.

External costs include:

- costs incurred under agreements with third-party CROs, CMOs and other third parties that conduct preclinical and clinical activities on our behalf and manufacture our product candidates;
- costs associated with acquiring technology and intellectual property licenses that have no alternative future uses; and
- other costs associated with our research and development programs, including laboratory materials and supplies and consulting fees.

Internal costs include:

- employee-related costs, including salaries, benefits and stock-based compensation expense, for our research and development personnel; and
- facilities and other expenses incurred in connection with our research and development programs, including expenses for allocated rent and facilities maintenance, and depreciation and amortization.

Research and development costs are expensed as incurred. In 2020, we did not track our internal indirect costs and external research and development costs by program. The intellectual property we licensed in late 2020 is fundamental to our platform and we did not focus on any specific programs. In the future, we expect to track research and development costs on a program by program basis as we identify the specific programs and product candidates to develop.

During 2020, we were eligible for a research and development tax credit. The tax incentive was available to us based on research and development activity within the United States and California during that year. These research and development tax incentives are recognized as a reduction to payroll tax expense when the right to receive has been attained and funds are collectible and are capped at $250,000 per year.

We expect our research and development expenses to increase substantially for the foreseeable future as we advance our product candidates into and through preclinical studies and clinical trials, pursue regulatory approval of our product candidates and expand our pipeline of product candidates. The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. The actual probability of success for our product candidates may be affected by a variety of factors, including the safety and efficacy of our product candidates, early clinical data, investment in our clinical programs, competition, manufacturing capability and commercial viability. We may never succeed in achieving regulatory approval for any of our product candidates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or if, when and to what extent we will generate revenue from the commercialization and sale of our product candidates, if approved by the FDA and other applicable authorities.

Our future research and development costs may vary significantly based on factors such as:

- the scope, rate of progress, expense and results of our clinical trials and preclinical development activities;
- the costs and timing of our CMC activities, including fulfillingGMP-related standards and compliance, and identifying and qualifying suppliers;
- per patient clinical trial costs;
- the number and duration of clinical trials required for approval of our product candidates;
- the number of sites included in our clinical trials;
- the countries in which the trials are conducted;
- delays in adding a sufficient number of trial sites and recruiting suitable patients to participate in our clinical trials;
- the number of patients that participate in the trials;
- patient drop-out or discontinuation rates;
- potential partial reimbursement from governmental agencies for our clinical activities;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;

- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates; the timing, receipt, and terms of any approvals from applicable regulatory authorities including the FDA and non-U.S. regulators;
- maintaining a continued acceptable safety profile of our product candidates following approval, if any, of our product candidates;
- significant and changing government regulation and regulatory guidance;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the extent to which we establish additional strategic collaborations or other arrangements; and
- the impact of any business interruptions to our operations or to those of the third parties with whom we work, particularly in light of the current COVID-19 pandemic environment.

General and Administrative

General and administrative expenses consist primarily of expenses related to employee-related costs, including salaries, benefits and stock-based compensation expense, for our executive, business development, finance and accounting, human resources and other administrative functions; legal services, including relating to intellectual property and corporate matters; accounting, auditing, consulting and tax services; insurance; and facility and other allocated costs not otherwise included in research and development expenses. We expect our general and administrative expenses to increase substantially for the foreseeable future as we anticipate an increase in our personnel headcount to support expansion of research and development activities, as well as to support our operations generally. We also expect an increase in expenses associated with being a public company, including costs related to accounting, audit, legal, regulatory, and tax-related services associated with maintaining compliance with applicable Nasdaq and SEC requirements; additional director and officer insurance costs; and investor and public relations costs.

Other Income (Expense), Net

Other income (expense), net includes interest expense incurred on our convertible notes and changes in the fair value of our redeemable convertible preferred stock tranche liabilities (see the subsection titled "—Critical Accounting Policies and Significant Judgments and Estimates" below and Notes 2, 8 and 12 to our financial statements included elsewhere in this prospectus for more details).

Results of Operations

Years Ended December 31, 2019 and 2020

The following table summarizes our condensed statements of operations and comprehensive loss for the years ended December 31, 2019 and 2020:

	Year Ended December 31,	
	2019	2020
	(in thousands)	
Operating expenses:		
Research and development	$ —	$ 9,123
General and administrative	29	4,377
Total operating expenses	29	13,500
Loss from operations	(29)	(13,500)
Other income (expense), net:		
Interest expense	(80)	(40)
Change in fair value of the redeemable convertible preferred stock tranche liability	—	(54,833)
Total other income (expense), net	(80)	(54,873)
Net loss and comprehensive loss	$ (109)	$ (68,373)

Research and Development Expenses

The following table summarizes our external and internal research and development expenses by nature for the year ended December 31, 2020 (in thousands):

External costs:	
CRO, CMO and other third-party preclinical and clinical trial costs	$ 3,127
Technology and intellectual property license(1)	2,822
Other research and development costs, including laboratory materials and supplies	1,060
Internal costs:	
Personnel-related expenses	1,357
Facilities and overhead expenses	757
Total research and development expenses	$ 9,123

(1) Primarily comprised of cost of common shares to be issued to Stanford under the License Agreement. For more details on this transaction, see Note 6 in our financial statements included elsewhere in this prospectus.

There were no research and development expenses incurred in the year ended December 31, 2019.

General and Administrative Expenses

In the year ended December 31, 2020, we incurred $4.4 million in general and administrative expenses, which comprised of (i) professional expenses of $1.7 million, primarily related to outside recruiting and marketing expenses; (ii) employee-related expenses of $1.3 million, which include salaries, benefits and stock-based compensation for our management and board members; and (iii) legal costs of $1.1 million.

Other Income (Expenses), Net

The other income (expenses), net in the year ended December 31, 2020 primarily comprised of the change in fair value of the redeemable convertible Series A redeemable convertible preferred stock tranche liabilities of

$54.8 million, as well as interest expense on the convertible note from a related party. See Note 12 to our financial statements included elsewhere in this prospectus for more details.

Unaudited Pro Forma Information

Our unaudited pro forma basic and diluted net loss per share for the year ended December 31, 2020 has been computed to give effect to (i) the conversion of all outstanding shares of our redeemable convertible preferred stock into shares of our common stock (ii) and the removal of gains or losses resulting from the re-measurement of the redeemable convertible preferred stock liabilities as the preferred stock will be exercised for shares of common stock immediately prior to the closing of this offering. Pro forma net loss per share does not include the obligation to issue 1,558,587 shares of our common stock to Stanford under the License Agreement, as these shares were not outstanding as of December 31, 2020. In addition, pro forma net loss per share does not include the shares expected to be sold in this offering.

The following table sets forth the computation of the unaudited pro forma basic and diluted net loss per share of common stock for the period presented:

	Year Ended December 31, 2020 (in thousands, except share and per share amounts)
Net loss attributable to common stockholders	$ (68,373)
Pro forma adjustment to reflect the removal of gains or losses resulting fromthe re-measurement of the redeemable convertible preferred stock tranche liabilities	54,833
Pro forma net loss	$ (13,540)
Weighted-average shares outstanding used in computing net loss per share attributable to common stockholders, basic and diluted	5,554,899
Pro forma adjustment to reflect the assumed conversion of the redeemable convertible preferred stock	30,019,945
Pro forma weighted-average shares outstanding used in computing pro forma net loss per share, basic and diluted	35,574,844
Pro forma net loss per share, basic and diluted	$ (0.38)

Liquidity and Capital Resources

We have incurred losses since inception and have incurred negative cash flows from operations from inception through December 31, 2020. As of December 31, 2020, we had $19.8 million of cash and cash equivalents and our accumulated deficit was $70.6 million. We have funded our operations to date primarily from the sale of redeemable convertible preferred stock and issuance of convertible promissory notes. Through March 31, 2021, we have raised $197.7 million in aggregate gross proceeds through such means.

Future Funding Requirements

Our primary uses of cash are to fund our operations, which consist primarily of research and development expenditures related to our programs and, to a lesser extent, general and administrative expenditures. We anticipate that we will continue to incur significant expenses for the foreseeable future as we continue to advance our product candidates, expand our corporate infrastructure, including the costs associated with being a public company, further our research and development initiatives for our product candidates, scale our laboratory and manufacturing operations, and incur marketing costs associated with potential commercialization. We are subject

to all of the risks typically related to the development of new drug candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Based upon our current operating plan, we estimate that our existing cash and cash equivalents as of the date of this prospectus, together with the estimated net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next months. Until we can generate a sufficient amount of revenue from the commercialization of our product candidates or from collaboration agreements with third parties, if ever, we expect to finance our future cash needs through public or private equity or debt financings, including this offering, collaborations and other strategic alliances and licensing arrangements, or any combination of these approaches. The sale of equity or convertible debt securities may result in dilution to our stockholders and, in the case of preferred equity securities or convertible debt, those securities could provide for rights, preferences or privileges senior to those of our common stock. Debt financings may subject us to covenant limitations or restrictions on our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our ability to raise additional funds may be adversely impacted by negative global economic conditions and any disruptions to and volatility in the credit and financial markets in the United States and worldwide that may result from the ongoing COVID-19 pandemic or other factors. There can be no assurance that we will be successful in acquiring additional funding at levels sufficient to fund our operations or on terms favorable or acceptable to us. If we are unable to obtain adequate financing when needed or on terms favorable or acceptable to us, we may be forced to delay, reduce the scope of or eliminate one or more of our research and development programs.

Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, results and costs of research and development, discovery, preclinical and non-clinical studies and clinical trials for our current and future product candidates;
- the number, scope and duration of clinical trials required for regulatory approval of our current and future product candidates;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities for our product candidates, including any requirement to conduct more studies or generate additional data beyond that which we currently expect would be required to support a marketing application;
- the cost of manufacturing clinical and commercial supplies of our current and future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the revenue, if any, received from commercial sales of any product candidates for which we may receive marketing approval;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payers;
- the costs to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing our patents or other intellectual property rights;

- expenses needed to attract, hire and retain skilled personnel;
- the costs of operating as a public company; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

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

Cash Flows

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

	Year Ended December 31,	
	2019	2020
	(in thousands)	
Net cash used in operating activities	$ (19)	$ (8,721)
Net cash used in investing activities	—	(1,545)
Net cash provided by financing activities	—	30,077
Net increase (decrease) in cash and cash equivalents	$ (19)	$19,811

Cash Flows from Operating Activities

Net cash used in operating activities was $8.7 million for the year ended December 31, 2020 and $19,000 for the year ended December 31, 2019.

Cash used in operating activities in the year ended December 31, 2020, was primarily due to our net loss for the year of $68.4 million adjusted by non-cash charges of $57.9 million and a net change of $1.7 million in our net operating assets and liabilities.The non-cash charges consisted of a $54.8 million change in the fair value of the redeemable convertible preferred stock tranche liabilities and $2.8 million for the shares of common stock issuable to Stanford pursuant to the License Agreement. The changes in our net operating assets and liabilities were primarily due to an increase of $2.5 million in accounts payable and accrued expenses, and $0.4 million increase in accrued compensation, offset by $1.2 million increase in prepaid expenses.

Cash Flows from Investing Activities

During the year ended December 31, 2020, cash used in investing activities was $1.5 million and related primarily to the purchase of lab equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2020 was $30.1 million, which consisted primarily of net proceeds from the issuance of shares of our Series A redeemable convertible preferred stock of $25.0 million ($24.8 million, net of issuance costs of $0.2 million) in two tranches, as well as $5.0 million from the issuance of a convertible note.

Recently Adopted Accounting Pronouncements

For information on new accounting standards, see Note 2 to our financial statements included elsewhere in this prospectus.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments at December 31, 2020:

	Payments Due by Period				
	Less than 1 Year	1 - 3 Years	3 - 5 Years	More than 5 Years	Total
	(in thousands)				
Operating lease obligations(1)	$ 209.2	$ —	$ —	$ —	$209.2
Stanford license agreement(2)	5.0	20.0	75.0	—	100.0
Total	$ 214.2	$ 20.0	$ 75.0	$ —	$309.2

(1) Consists of our corporate headquarters lease in South San Francisco, California that expires in June 2021. The operating lease obligations above do not include our obligations under the new lease we entered into in January 2021. See Note 14 to our financial statements included elsewhere in this prospectus.

(2) Represents annual license maintenance fees under the exclusive license agreement with Stanford. The table above does not include the maintenance fees for the periods after year six as the timing and likelihood of commercial sale is unknown and hard to estimate. In addition, these amounts do not include any potential contingent payments, including those due upon the achievement by us of specified clinical, regulatory and commercial milestones, as applicable, or patent prosecution, and royalty payments we may be required to make under this agreement. 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. For more information about potential payments thereunder, see Note 6 to our financial statements included elsewhere in this prospectus.

We enter into contracts in the normal course of business with CROs for clinical trials, with CMOs for the manufacture of clinical supplies and with other vendors for preclinical studies, supplies and other services and products for operating purposes. These contracts generally provide for termination on notice or may have a potential termination fee if a purchase order is cancelled within a specified time, and therefore are cancelable contracts and not included in the table above.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including but not limited to those related to accrued research and development costs, the fair value of derivative redeemable convertible preferred stock tranche liabilities, the fair value of redeemable convertible preferred stock and common stock and stock-based compensation expense, the valuation of deferred tax assets, and uncertain income tax positions. We base our estimates on historical experience, known trends and events and various other factors that are believed to be 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. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our financial statements included elsewhere in this prospectus, we believe the following accounting policies and estimates to be most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Expenses

We have entered into various agreements with CMOs and may enter into contracts with CROs in the future. As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel and third parties to identify services that have been

performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued research and development expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We accrue for costs related to research and development activities based on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors, including CROs and CMOs, that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received. We make significant judgments and estimates in determining accrued research and development liabilities as of each reporting period based on the estimated time period over which services will be performed and the level of effort to be expended. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Redeemable Convertible Preferred Stock Tranche Liability

We utilize the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value each preferred stock tranche liability. On a quarterly basis, we assess these assumptions and estimates as additional information impacting the assumptions is obtained. Estimates and assumptions impacting the fair value measurement include the fair value of the preferred stock, the expected term when the tranche liability will be settled, expected volatility, risk-free interest rate, and expected dividend yield.

We determine the fair value per share of the underlying preferred stock by taking into consideration our most recent sales of our preferred stock as well as additional factors that we deem relevant. We are a private company and lack company-specific historical and implied volatility information of our stock. Therefore, we determine expected stock volatility based on the historical volatility of publicly traded peer companies. We estimate the risk-free interest rate by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the outstanding tranche liability. We have assumed a 0% dividend considering that our board of directors has no history of declaring dividends and does not intend to declare.

As of December 31, 2020, we had outstanding tranche liability of $29.1 million related to the third tranche of the Series A redeemable convertible preferred stock, which subsequently settled on February 16, 2021. See Note 14 to our financial statements included elsewhere in this prospectus.

Stock-Based Compensation Expense

Our stock-based equity awards include restricted stock awards and stock options that are granted to employees and consultants and accounted for at fair value on the award grant date. Stock-based compensation expense is recognized over the awards' vesting period on a straight-line basis and recorded as either research and development or general and administrative expenses in the statements of operations and comprehensive loss based on the function to which the related services are provided. Forfeitures are accounted for as they occur.

The Black-Scholes option-pricing model, used to estimate fair value of stock-based awards, requires the use of the following assumptions:

- *Fair Value of Common Stock*—See the subsection titled "—Common Stock Valuations" below for more information.
- *Expected Term*—The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term for our stock options was calculated based on the weighted-average vesting term of the awards and the contract period, or simplified method.
- *Expected Volatility*—Since we are not yet a public company and do not have any trading history for our common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their size, stage in the life cycle or area of specialty. We will continue to apply this process until enough historical information regarding the volatility of our stock price becomes available.
- *Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.
- *Expected Dividend Yield*—We have never paid dividends on the common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. See Notes 2 and 10 to our financial statements included elsewhere in this prospectus for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted in the year ended December 31, 2020.

As of December 31, 2020, the unrecognized stock-based compensation expense related to stock options was $2.9 million and is expected to be recognized as expense over a weighted-average period of approximately 3.7 years. We expect to continue to grant stock options and other equity-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

The intrinsic value of all outstanding stock options as of , 2021 was approximately $ million, based on the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, of which approximately $ million related to vested share-based awards and approximately $ million related to unvested share-based awards.

Common Stock Valuations

We are required to estimate the fair value of the common stock underlying our equity awards when performing fair value calculations. The fair value of the common stock underlying our equity awards was approved on each grant date by our board of directors. The fair value of our common stock was determined by management, considering input from independent third-party valuation analyses. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. In the absence of a public trading market for our common stock, on each grant date we develop an estimate of the fair value of our common stock in order to determine an exercise price for the option grants. Our determinations of the fair value of our common stock were made using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide: *Valuation of Privately Held Company Equity Securities Issued as Compensation* (the Practice Aid). Because shares of our common stock are not publicly traded, estimating their fair values can be highly complex and subjective.

Management considered various objective and subjective factors to determine the fair value of our common stock, including:

- valuations of our common stock performed with the assistance of independent third-party valuation specialists;
- our stage of development and business strategy, including the status of research and development efforts of our product candidates, and the material risks related to our business and industry;
- our results of operations and financial position, including our levels of available capital resources;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- the lack of marketability of our common stock;
- the prices of our redeemable convertible preferred stock sold to investors in arm's length transactions and the rights, preferences and privileges of our redeemable convertible preferred stock relative to those of our common stock;
- the likelihood of achieving a liquidity event for the holders of our common and redeemable convertible preferred stock, such as an initial public offering or a sale of our Company, given prevailing market conditions;
- trends and developments in our industry; and
- external market conditions affecting the life sciences and biotechnology industry sectors.

The Practice Aid prescribes several valuation approaches for setting the value of an enterprise, such as the cost, income and market approaches, and various methodologies for allocating the value of an enterprise to our common stock. The cost approach establishes the value of an enterprise based on the cost of reproducing or replacing the property less depreciation and functional or economic obsolescence, if present. The income approach establishes the value of an enterprise based on the present value of future cash flows that are reasonably reflective of our future operations, discounting to the present value with an appropriate risk adjusted discount rate or capitalization rate. The market approach is based on the assumption that the value of an asset is equal to the value of a substitute asset with the same characteristics. Each valuation method was considered in our analysis.

For our valuation performed as of June 30, 2020, in accordance with the Practice Aid, we utilized an Option Pricing Method (OPM), based analysis (primarily the OPM Backsolve methodology) to determine the estimated fair value of our common stock as we concluded it was the most appropriate method to utilize based on our stage of development and other relevant factors. Within the OPM framework, the Backsolve method for inferring the total equity value implied by a recent financing transaction involves the construction of an allocation model that takes into account our capital structure and the rights and preferences of each class of stock, then assumes reasonable inputs for the other OPM variables (expected time to liquidity, volatility, risk-free rate, etc.). The total equity value is then iterated in the model until the model output value for the equity class sold in a recent financing round equals the price paid in that round. The OPM is generally utilized when specific future liquidity events are difficult to forecast, i.e., the enterprise has many choices and options available, and the enterprise's value depends on how well it follows an uncharted path through the various possible opportunities and challenges. In determining the estimated fair value of our common stock, management also considered the fact that our stockholders could not freely trade our common stock in the public markets. Accordingly, we applied discounts to reflect the lack of marketability of our common stock based on the weighted-average expected time to liquidity. The estimated fair value of our common stock at each grant date reflected a non-marketability discount partially based on the anticipated likelihood and timing of a future liquidity event.

For valuations performed after June 30, 2020, in accordance with the Practice Aid, we utilized a hybrid method that combined the Probability-Weighted Expected Return Method (PWERM), and the OPM, as we

concluded these were the most appropriate methods to utilize based on our stage of development and other relevant factors. The PWERM is a scenario-based analysis that estimates the value per share of common stock based on the probability-weighted present value of expected future equity values for the common stock, under various possible future liquidity event scenarios, considering the rights and preferences of each class of stock, discounted for a lack of marketability. Under the hybrid method, an OPM Backsolve was utilized to determine the fair value of our common stock in certain of the PWERM scenarios (capturing situations where our development path and future liquidity events were difficult to forecast) and potential initial public offering exit events were explicitly modeled in the other PWERM scenarios. A discount for lack of marketability was applied to the value derived under each scenario to account for a lack of access to an active public market.

We also considered the amount of time between the independent third-party valuation dates and the grant dates and performed an interpolation of the fair value between the two valuation dates to estimate common stock fair value at each grant date. This determination included an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

Following the completion of this offering, the fair value of our common stock will be based on the closing quoted market price of our common stock as reported on the date of grant on the primary stock exchange on which our common stock is traded. Estimating the fair value of our common stock will not be necessary to determine the fair values of new awards once the underlying shares begin trading.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Quantitative and Qualitative Disclosures About Market Risk

The primary objectives of our investment activities are to ensure liquidity and to preserve capital. We are exposed to market risks in the ordinary course of our business. Our primary risks include interest rate sensitivities.

Interest Rate Risk

We had cash and cash equivalents and of $19.8 million as of December 31, 2020 which consisted of bank deposits and highly liquid money market funds. To minimize the risk in the future, we intend to maintain our portfolio of cash equivalents in institutional market funds that are composed of U.S. Treasury and U.S. Treasury-backed repurchase agreements or short-term U.S. Treasury securities. We do not believe that inflation, interest rate changes, or exchange rate fluctuations had a significant impact on our results of operations for any periods presented herein.

Foreign Currency Exchange Risk

All of our employees and our operations are currently located in the United States and our expenses are denominated in U.S. dollars. We therefore are not currently exposed to significant market risk related to changes in foreign currency exchange rates. However, we have contracted with and may continue to contract with non-U.S. vendors who we may pay in local currency. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. We believe a hypothetical 1% chance in exchange rates during any of the periods presented would not have a material effect on our consolidated financial statements included elsewhere in this prospectus.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and in the future our clinical trial costs. We believe that inflation has not had a material effect on our consolidated financial statements included elsewhere in this prospectus.

Emerging Growth Company and Smaller Reporting Entity Status

We are an "emerging growth company," as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay the adoption of new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for emerging growth companies include presentation of only two years of audited financial statements in a registration statement for an initial public offering, an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404 of SOX, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation and less extensive disclosure about our executive compensation arrangements. We have elected to use the extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that (i) we are no longer an emerging growth company or (ii) we affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. However as described in Note 2 to our financial statements included elsewhere in this prospectus, we early adopted certain accounting standards, as the JOBS Act does not preclude an emerging growth company from adopting a new or revised accounting standard earlier than the time that such standard applies to private companies to the extent early adoption is permitted. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest of (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) the last day of our fiscal year following the fifth anniversary of the completion of this offering, (iii) the date on which we are deemed to be a "large accelerated filer," under the rules of the SEC, which means the market value of equity securities that is held by non-affiliates exceeds $700.0 million as of the prior June 30th and (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

If we are a "smaller reporting company" at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

BUSINESS

Overview

We are a clinical-stage, next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to potentially cure a wide range of serious and life-threatening diseases. We are pioneering a precision gene editing approach to achieve one of medicine's most elusive goals: to precisely "find & replace" any gene in the genome. Our next-generation gene editing platform allows us to precisely correct mutations, replace entire disease-causing genes with normal genes, or insert new genes into predetermined, safe locations. We believe our approach could enable nearly limitless applications to transform human health, including directly correcting mutations, engineering cells to permanently deliver therapeutic proteins, and precisely engineering effector cells to treat or cure a wide range of serious genetic and other diseases, including cancer, autoimmune and neurodegenerative diseases.

Our lead product candidate GPH101 is a highly differentiated approach with the potential to directly correct the mutation that causes SCD and restore normal HgbA expression. Curing sickle cell disease by correcting the disease-causing point mutation to normal is viewed as the gold-standard for curing SCD and has been the dream of treating physicians for generations. We have received clearance of our IND and we intend to enroll the first patient in a Phase 1/2 clinical trial of GPH101 in . We are also advancing our research programs and pipeline of potentially one-time curative therapies for a wide range of genetic and other serious diseases and intend to file an IND for a second program by .

Our technology builds on first-generation proven CRISPR technology to achieve high rates of targeted gene integration. Our technology was developed in the Stanford laboratories of our two scientific founders, both pioneers in gene therapy and gene editing: Matthew Porteus, M.D., Ph.D., and Maria Grazia Roncarolo, M.D. Dr. Porteus is considered to be one of the founders of the field of gene editing and was a scientific founder of CRISPR Therapeutics. He was the first to demonstrate that an engineered nuclease could be used to correct genes by harnessing precision cellular DNA repair machinery. Dr. Roncarolo is a pioneer in multipotent HSC gene therapy and her work led to the first approved HSC gene therapy product. She established and is Director of the Stanford Center for Definitive and Curative Medicine to treat patients with currently incurable diseases through the development of innovative stem cell- and gene-based therapies. Drs. Porteus and Roncarolo, both practicing physicians, came together with the conviction that targeted gene integration could lead to an entirely new class of potentially curative therapies.

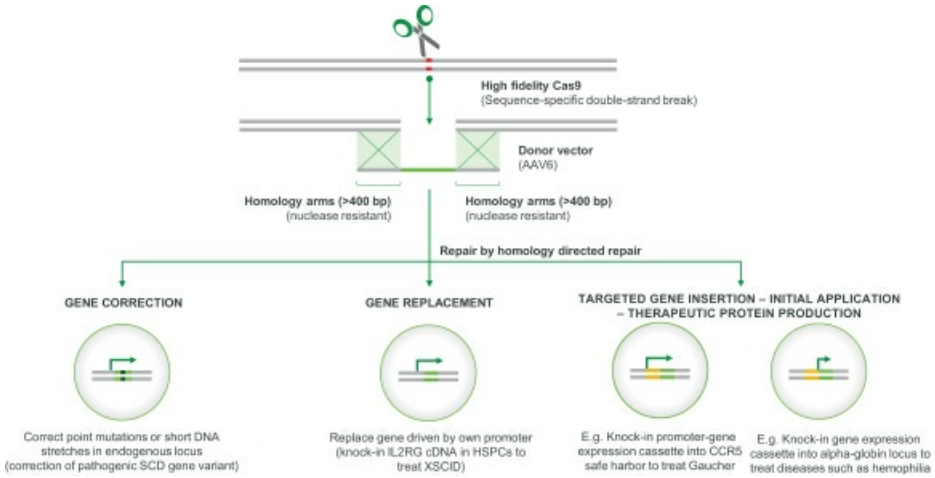
Our approach has broad therapeutic applications and has enabled high efficiency targeted gene integration in a wide range of primary human cell types. In our initial programs, we apply our approach *ex vivo* in a patient's own HSCs which are reinfused after gene integration (autologous HSCT). HSCs are multipotent stem and progenitor cells that can give rise to all cells of the blood and immune system and have proven their curative potential across dozens of diseases as demonstrated by allo-HSCT.

Our approach can be thought of as "find & replace," using CRISPR to find a target gene and HDR to replace DNA in the target gene with DNA copied from a template. We create a precise incision in a target gene using a modified, high fidelity CRISPR-based nuclease and then induce conditions in target cells that overwhelmingly favor HDR, a natural and precise cellular DNA repair process. Using a non-integrating AAV6 vector, we deliver a donor DNA template strand to the target gene which is copied via HDR to create a new coding strand. We then apply our HSC biology expertise to optimally engineer and manufacture HSCs, a historically intractable cell type for harnessing HDR. Using our next-generation gene editing approach, we have achieved gene integration efficiencies in excess of curative thresholds and demonstrated preclinical proof-of-concept across multiple diseases models. Beyond GPH101, our pipeline includes multiple programs including GPH201 for XSCID, our first gene replacement program, and GPH301 for Gaucher disease, our first targeted gene insertion program, and multiple undisclosed programs in both HSCs and other cell types.

Our approach differs from first generation gene and base editing technologies due to:

- **Direct targeting and correction of genetic lesions:** We harness HDR to replace the disease-causing mutation or the entire disease-causing gene with the normal, wild-type genetic sequence. This is in contrast to first generation gene editing approaches that have focused on knocking-out genes.
- **Efficiency of targeted gene integration:** In our GPH101 sickle cell gene correction program, we have demonstrated up to approximately 70% gene correction efficiency in HSPCs in *ex vivo* studies. In gene replacement and targeted gene insertion applications, we have consistently demonstrated efficiencies of approximately 30-50% in HSPCs across a range of gene targets and templates. We believe these efficiencies are above the curative threshold for a broad array of indications, including SCD. Prior to the development of our gene integration platform efficiencies using HDR in HSPCs were approximately 10%.
- **Breadth of applications:** We can replace genes of up to 4 kb allowing us to correct not only single point mutations but also multiple mutations within the same gene, and to address gene deletions. We can also precisely insert genes under control of a native promoter for naturally regulated expression, into a safe harbor location under the control of an exogenous promoter, or under the control of a lineage specific cellular promoter.
- **Uniquely suited to expand the patient population eligible for potential one-time curative HSC therapies:** We believe that the high efficiency and precision of our targeted gene integration platform could potentially reduce threshold bone marrow engraftment levels. This could potentially obviate the need for full chemotherapeutic myeloablative bone marrow conditioning (the current standard for allo-HSCT and most gene editing and gene therapy approaches in development). In addition, our approach avoids the theoretical risk of insertional oncogenesis from integrating viral vectors and incorporates a high fidelity CRISPR-based nuclease, for potentially improved safety. Pairing these advantages with targeted and safer bone marrow conditioning could bring HSC-based curative therapies to much larger numbers of patients.

We are applying our technology in three settings: Gene Correction, Gene Replacement, and Targeted Gene Insertion.



Gene Correction

Our approach allows us to precisely correct pathogenic genes by directly targeting and correcting the specific disease-causing mutation to restore the normal, wild-type sequence.

We are developing GPH101, our lead product candidate for SCD, which is designed to directly correct the genetic mutation responsible for SCD. The mortality and morbidity associated with SCD, all caused by a single mutation, has made curing SCD a dream of many clinicians. Multiple genetic therapies are in development to address SCD, but due to technical limitations, these therapies are primarily focused on expressing alternate hemoglobin genes such as fetal hemoglobin or a transgenic hemoglobin. Our approach is the first in industry to directly correct the SCD-causing mutation to restore normal adult hemoglobin expression. Under IND-enabling GMP manufacturing conditions, we can precisely correct the SCD mutation in over 55% of treated cells, which we believe can achieve the threshold required to cure patients (engraftment of 20% corrected cells). These treated HSPCs are fully functional and can engraft *in vivo* in a humanized mouse, and can produce functionally normal red blood cells expressing normal adult hemoglobin *ex vivo.* Furthermore, we have demonstrated in a mouse model of SCD that our approach significantly increased normal HbA expression, extended RBC lifespan from two days in sickle mice to up to 19 days in gene corrected mice, and eliminated RBC sickling. We believe this data supports the curative potential of our approach. We have received clearance of our IND and intend to enroll the first patient in a Phase 1/2 trial of GPH101 in .

Gene Replacement

Our gene replacement approach allows us to replace dysfunctional genes with a new normal copy of an entire gene at its normal location in the chromosome.

We are developing GPH201 for the treatment of XSCID, a rare, life-threatening disease where multiple mutations in a single gene (IL2RG) prevent normal immune system function. In preclinical studies, we demonstrated that GPH201 treatment of HPSCs from healthy donors led to a consistent rate of IL2RG gene replacement of greater than 40%. Furthermore, treatment of HSPCs from an XSCID patient led to a significant increase in the number of T cells and natural killer (NK) cells, in *in vitro* differentiation assays and in a mouse model, consistent with a reversal of the XSCID phenotype. We believe our gene replacement approach leading to normal regulated expression of the IL2RG gene could be an optimal cure for XSCID. We believe that the survival advantage of the progeny of gene edited cells combined with our high efficiency of gene replacement could enable patients to benefit from GPH201 without undergoing chemotherapy-based conditioning. We have an agreement to investigate the potential use of a clinical-stage non-genotoxic HSC targeted antibody-based bone-marrow conditioning (non-genotoxic HSC targeted conditioning) regimen with GPH201. We believe that GPH201 will generate preliminary data on combining our autologous HSC therapies with non-genotoxic HSC targeted conditioning, and our clinical experience could accelerate our ability to use non-genotoxic HSC targeted conditioning with our other product candidates.

Targeted Gene Insertion

Our technology enables the targeted insertion of entire gene cassettes into chosen chromosomal locations. We believe that this could have broad therapeutic applications by allowing for permanent production of therapeutic proteins and enzymes, in specific cell lineages, and from targeted genomic locations. This prevents the variability in gene expression, and the potential risk of insertional oncogenesis which are limitations of random gene integration approaches using LVV. Permanent therapeutic protein production applications of HSC targeted integration include expression of proteins and enzymes in target organs including the CNS by tissue resident HSC-derived myeloid cells, as well as efficient systemic delivery of secreted proteins in the circulation. Potential applications include enzyme replacement for metabolic disease, CNS delivery of therapeutic proteins or antibodies for neurodegenerative diseases, and production of plasma proteins for coagulation and complement disorders.

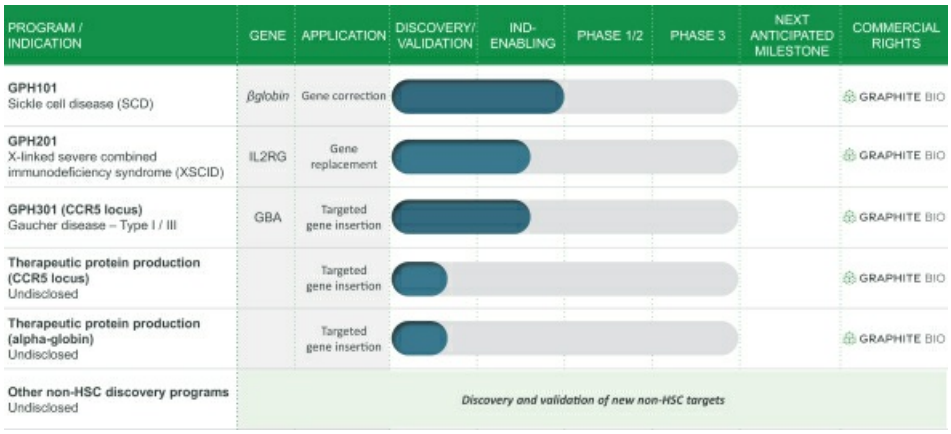
We currently harness two genomic locations for targeted insertion, the CCR5 safe harbor locus and the alpha globin locus:

Our lead product candidate from our CCR5 locus technology is GPH301, which we are developing for the treatment of Gaucher disease. With GPH301, we are inserting a functional copy of the GCase gene into the CCR5 chromosomal locus. This locus is known as a "safe harbor" both because of the lack of deleterious effects associated with gene insertions that occur there and because the expression of inserted genes can be reliably and precisely controlled by regulatory elements inserted together with the gene of interest. We use a lineage specific promoter so that GCase expression is limited to monocytes and macrophages which can migrate into tissues including crossing the blood brain barrier into the CNS. We inserted GCase into approximately 35% of targeted CCR5 alleles in HSPCs (resulting in ~50% of cells having at least one allele targeted) which subsequently engrafted, differentiated, and expressed GCase from macrophages at levels which could lead to a functional cure. This same approach can be used for therapeutic protein production in many other diseases including other lysosomal storage diseases. We believe that proof of concept in Gaucher can accelerate development of a CCR5 safe harbor protein production pipeline. We believe there are significant synergies and regulatory efficiencies because these programs will use the same RNA guide and preclinical safety assessment.

Our other approach for therapeutic protein production harnesses the alpha-globin locus, which uses the alpha-globin promoter to express high protein levels from the red blood cell lineage and normalize plasma protein levels to potentially develop HSC-based cures and treatments for additional indications.

We intend to pursue applications of our technology platform to develop potential therapies for a number of serious diseases. Our high efficiency gene editing technology has been shown using human cells and/or animal models to be applicable to a broad range of HSC-based indications (e.g. MPS1, Krabbe, beta-thalassemia) as well as other tissues, such as airway stem cells (cystic fibrosis), neural stem cells, pluripotent stem cells and keratinocytes (wound healing). We intend to investigate the potential of developing therapies for other diseases based on these findings.

Our Pipeline



Our Team and Investors

Our team is led by executives who have deep experience in drug development and company-building in the biopharmaceutical industry. Josh Lehrer, M.D., our Chief Executive Officer, previously served as chief medical officer at Global Blood Therapeutics (GBT), where he led development for the marketed SCD treatment Oxbryta™ from pre-IND stages through its commercial launch. Prior to GBT, he served in clinical roles at Genentech and as a practicing cardiologist at Stanford. Katherine Stultz, our Chief Operating Officer, has extensive experience in developing brands and building teams, as a global project leader and general manager at Celgene and in early commercialization roles at Eli Lilly. Jerry Cacia, our Chief Technical Officer, most recently served as head of global technical development at Roche/Genentech, where he supported a pipeline that included over 80 new molecular entities and more than 100 development projects in various stages, including a number of cell and gene therapies. Philip Gutry, our Chief Business Officer and Head of Finance & Investor Relations, previously served as Chief Business Officer at Kronos Bio and in senior business development and finance roles at Regeneron, MPM Capital, and Gilead. We are building a broader team that is passionate about our mission of urgently translating groundbreaking science to transform lives. Our people function is led by SVP Julia Tran, a three-time executive with more than 20 years of experience in building and growing companies in the biotechnology industry including Amyris, Inc., CV Therapeutics, Inc. and Millennium Pharmaceuticals Inc. and in technology companies including vArmour Networks, SilverTail Systems and most recently Blue Lava where she was a founder, Chief Operating Officer and Chief Community Officer.

Since our inception, we have raised approximately $197.7 million in funding from leading investors, including Cormorant Asset Management, Deerfield Management Company, Federated Hermes Kaufmann Funds, Fidelity Management & Research Company, Janus Henderson Investors, Logos Capital, OrbiMed, Perceptive Advisors, RA Capital, Rock Springs Capital, Samsara BioCapital, Surveyor Capital (a Citadel company), Venrock Healthcare Capital Partners, and our founding investor Versant Ventures. Stanford University also participated in our Series B preferred stock financing in March 2021.

Our Strategy

We are a next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to cure a wide range of serious and life-threatening diseases. Our goal is to advance a portfolio of one-time curative therapies which can ultimately be administered in the outpatient setting. The key components of our strategy are as follows:

- **Rapidly demonstrate clinical proof-of-concept for gene correction with our lead product candidate, GPH101, for the treatment of sickle disease.** Our lead product candidate, GPH101, which we believe is the first approach in our industry to directly correct the SCD-causing mutation to restore normal adult hemoglobin expression. We have shown gene correction rates, engraftment, and effects in preclinical models all supporting the curative potential of our approach. Under IND-enabling GMP manufacturing conditions, we can precisely correct the SCD mutation in over 55% of treated cells, which we believe can achieve the threshold required to cure patients (engraftment of 20% corrected cells). We have received clearance of our IND and intend to enroll the first patient in a Phase 1/2 trial in . We believe that this program will serve as proof-of-concept for our overall platform and for the ability to precisely correct a dysfunctional gene by directly correcting the specific mutation and restoring the normal genotype.
- **Expeditiously advance the gene replacement application of our technology with GPH201 for the treatment of XSCID.** We are developing GPH201 for the treatment of XSCID, where multiple mutations in a single gene prevent normal immune system function. In preclinical studies, we demonstrated that GPH201 treatment of HSPCs from healthy donors led to a consistent rate of gene replacement of greater than 40% and immune reconstitution in a mouse model. We believe that this program will serve as proof-of-concept for our platform's ability to replace a dysfunctional gene with a new normal copy of an entire gene at its normal chromosomal location.

- **Establish the broad potential of targeted gene insertion with GPH301 for the treatment of Gaucher disease.** By precisely integrating genes into the CCR5 "safe harbor" locus or into the alpha globin locus, we can insert genes precisely to permanently produce therapeutic proteins to potentially address many diseases of protein deficiency. Initially, we intend to develop GPH301 for the treatment of Gaucher disease, caused by a deficiency in the glucocerebrosidase (GCase) enzyme, which we believe will establish proof-of-concept for therapeutic protein production and allow us to rapidly expand into other indications, including other lysosomal storage diseases. We have demonstrated that GPH301 treatment of HSPCs resulted in approximately 35% insertion and normal GCase production , which we believe can potentially be curative. Our other therapeutic protein production approach uses the alpha-globin locus to express high protein levels from the red blood cell lineage and normalize plasma protein levels to potentially develop HSC-based cures and treatments for additional indications.

- **Expand the patient population and indications eligible for one-time curative HSC therapies by harnessing industry advances in non-genotoxic HSC targeted conditioning regimens.** We believe that the high efficiency and precision of our targeted gene integration platform can reduce threshold bone marrow engraftment levels. This could potentially obviate the need for full chemotherapeutic myeloablative bone marrow conditioning (the current standard for allo-HSCT and most gene editing and gene therapy approaches in development). We have an agreement to investigate the potential use of a clinical-stage non-genotoxic HSC targeted conditioning regimen with GPH201. We believe that GPH201 will generate preliminary data on combining our autologous HSC therapies with non-genotoxic HSC targeted conditioning, and our clinical experience could accelerate our ability to use non-genotoxic HSC targeted conditioning with our other product candidates.

- **Leverage high efficiency targeted gene integration in other cell types.** We have demonstrated vast potential for our technology across a wide range of cell types. Our platform has been shown to achieve high and potentially therapeutic targeted gene integration efficiencies, and in some cases preclinical efficacy, in airway stem cells, keratinocytes, mesenchymal stem cells, neural stem cells, pluripotent stem cells, and T-cells. We intend to advance research programs in these cell types with a focus on developing highly differentiated therapeutics which can address serious diseases.

- **Continue to optimize and expand our next-generation gene editing technology to reinforce our leadership in targeted gene integration.** We have established a leading position in targeted gene integration by building on the pioneering work of our founders and technologies licensed from Stanford. We are continuing to build our research organization with particular focus on HDR platform improvements, advancing new pipeline targets in HSCs and effector cells, and discovering next generation targeted integration technologies and delivery systems.

- **Evaluate potential strategic collaborations to maximize the broad therapeutic potential of our technology and product candidates.** Given the broad applicability of our technology and differentiated product candidates to address serious genetic diseases, we plan to selectively evaluate, and if appropriate, enter into strategic collaborations to maximize their potential. We may selectively collaborate with potential future partners that provide us with complementary technologies or resources that could accelerate our programs or expand into new applications.

Current Approaches to Gene Therapy and Gene Editing and Their Limitations

Background on Genetic Disorders

A genetic disorder is a disease caused by an abnormal change in a person's DNA. Most genetic disorders are caused by a mutation in a single gene (monogenic disorder) which results in deficient or defective protein function. These mutations come in many different forms, including:

- Single point mutations—caused by a single base point mutation that causes a "misspelling" in diseases such as SCD.

- Multiple point mutations in the same gene—in diseases such as XSCID.
- Gene deletions—most or all of a gene is missing, in diseases such as beta-thalassemia.
- Gene expansion—extra abnormal DNA is inserted in diseases such as Huntington's disease.

Mutations that cause genetic disease can either cause loss of function or a toxic gain of function of an important protein. For example, XSCID is caused by lack of functional IL2RG protein, Gaucher is caused by loss-of-function mutations in the GBA1 gene leading to dysfunctional GCase, and cystic fibrosis is caused by the lack of functional CFTR protein. Examples of toxic gain of function, where mutations can cause a protein to have an abnormal and disease-causing function include SCD where sickle hemoglobin (HgbS) injures red blood cells, or Huntington's disease where the huntingtin proteins injure neurons.

Evolution of Genetic Medicines

Genetic medicines have advanced rapidly over the past decade. Initial gene addition approaches have yielded multiple approved products. CRISPR-Cas9 approaches for gene knock-outs are now being translated into the clinic. Base editing builds upon CRISPR-Cas9 and enables targeted editing of certain point mutations.

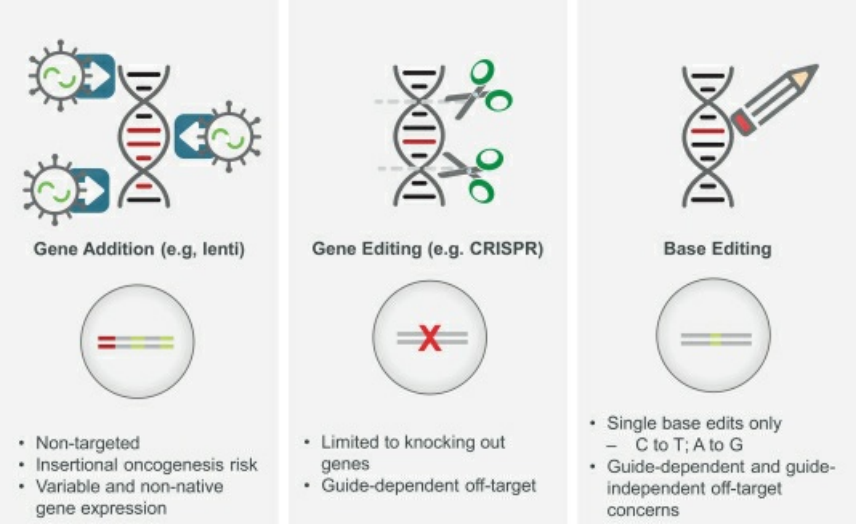


Figure: Evolution of Genetic Medicines

Gene Addition

In gene addition, a functional copy of a normal gene is introduced into a cell, typically by a non-integrating viral vector, to drive expression of a normal protein. Recently approved therapies use this approach for spinal muscular atrophy and mutation-associated retinal dystrophy. Other approaches use viral vectors, such as retroviruses and LVV, which randomly integrate a therapeutic gene into the genome for permanent expression.

The principal limitations of gene addition approaches are:

- limited durability for non-integrating viral vectors;
- risk of insertional oncogenesis for permanent integrating viral vector (e.g. LVV);

- variability in vector copy number per cell leading to variable gene expression;
- lack of normal endogenous regulation of gene expression;
- inability to correct the disease-causing mutation; and
- potentially curative only for loss of function mutations.

Gene Editing

Gene editing approaches using CRISPR-Cas9 or similar CRISPR nuclease-based technologies are in, or will shortly be initiating, clinical development. CRISPR-Cas9 creates double-stranded breaks in DNA which can be repaired in two primary ways: 1) non-homologous end joining (NHEJ) which creates targeted insertions or deletions (INDELs) or 2) HDR, which can precisely replace DNA at the target cut site by copying from a template. When CRISPR was first shown to be a gene editing tool in human cells, the primary goal and most powerful anticipated application was to use CRISPR with HDR to allow precise gene correction, replacement and insertion. However, repair following CRISPR overwhelmingly favors NHEJ, and due to technical challenges and limitations, efficient use of HDR was not possible in human cells. For this reason current CRISPR nuclease-based technology is being developed using NHEJ to create INDELs which cannot repair genes, but can alter gene expression. Because RNA guides are used to target Cas9 enzyme (or other CRISPR nucleases) to specific DNA sites, gene editing has much higher precision than earlier methods of permanently modifying the genome, such as gene addition by viral vector integration, and reduces the theoretical risks of insertional oncogenesis with these methods.

CRISPR-Cas9 mediated INDEL (insertions or deletion of bases in an organism's genome) formation is well suited to introducing new mutations that can disrupt and knock out a target gene. Because the vast majority of genetic diseases are caused by a mutation resulting in loss of function of an important protein, CRISPR INDEL approaches to potentially cure genetic diseases generally require an indirect approach to treat disease and are not able to directly correct the disease-causing mutation. For instance, in SCD, emerging approaches in preclinical and clinical development attempt to knock out Bcl11a function in order to induce fetal hemoglobin expression, rather than directly correcting the point mutation in sickle globin which causes SCD. Three programs using CRISPR INDEL approaches are currently in clinical development of which one program has provided initial clinical validation for the safety and potential efficacy of using such approaches for autologous cell therapies.

The principal limitations of gene editing using CRISPR-Cas9 are:

- introduces new mutations at the target;
- generally requires an indirect approach (i.e. knocking out another gene rather than fixing the disease causing gene); and
- an indirect approach may provide clinical benefit but is unlikely to be the optimal curative approach to most serious genetic diseases.

Base Editing

Base editing harnesses CRISPR-Cas9 to deliver a deaminase to a target DNA site, resulting in making a single nucleotide change in the target DNA. This is potentially an advance over nuclease only approaches because it allows direct targeting of a subset of mutations that cause genetic disease. To our knowledge, no base editors have entered clinical development.

The principal limitations of base editing are:

- base editing programs currently in development can only correct two of six potential nucleotide changes (e.g. cannot change A to T (adenine to thymine) as is required to correct the sickle mutation and convert sickle hemoglobin to normal adult hemoglobin);

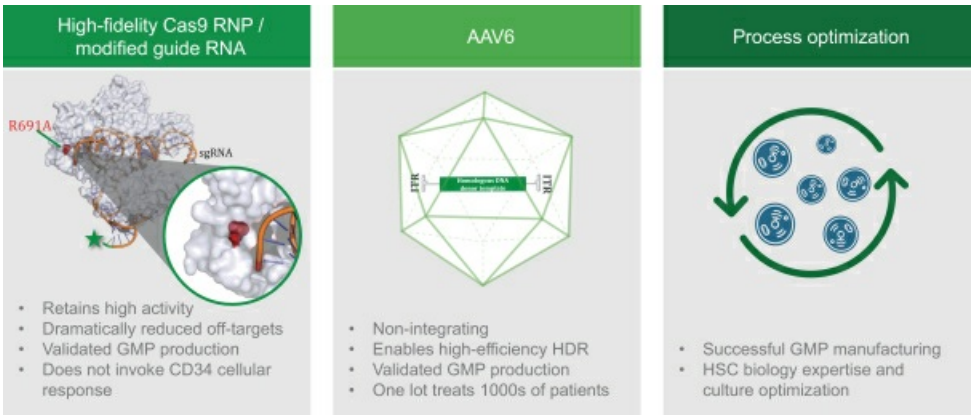
- can only correct or introduce a single point mutation at a time; and
- guide-independent potential off target risks to both DNA and RNA resulting from deaminases modifying bases which are not being targeted.

Our Next-Generation Gene Editing Approach

Our approach builds on the precision and clinical validation for current gene editing approaches to achieve an entirely new outcome—high efficiency targeted gene integration. This has the potential to expand the therapeutic opportunities for gene editing beyond conventional gene editing and base editing to enable efficient correction of any type of disease-causing genetic lesion. Beyond gene correction and replacement, this approach is designed to allow the insertion of new therapeutic genes into cells with significantly greater precision and efficiency than existing approaches. We believe this enables broad therapeutic applications ranging from correcting mutations, engineering cells to permanently deliver therapeutic proteins, and precisely engineering effector cells to treat or cure a wide range of serious genetic and other diseases, including cancer, autoimmune and neurodegenerative diseases.

Our innovative approach is a new platform technology built using our deep stem cell biology experience and proven CRISPR technology to efficiently harness a high-fidelity DNA repair process called HDR to integrate DNA copied from a DNA template into genes. Our approach can be described as "find & replace." We employ CRISPR technology to find and cut a target gene and harness HDR to "copy and paste" replacement DNA from a template. We have demonstrated high efficiency targeted gene integration across numerous cell types and curative potential in multiple animal models.

Our next generation gene editing technology creates a precise incision in a target gene using a modified, high fidelity CRISPR-based nuclease and we then induce conditions in target cells that overwhelmingly favor DNA repair by a mechanism that relies on HDR rather than the less desirable and more error-prone repair mechanism known as non-homologous end joining or NHEJ. HDR repairs DNA using a DNA template and results in high fidelity copying of template DNA into the correction site while reducing the introduction of DNA mutations that occur with first generation NHEJ gene editing approaches. We achieve HDR-mediated repair by using a non-integrating AAV6 viral vector to deliver template DNA (also called donor DNA) to the target gene. The donor DNA contains 400 base pair DNA segments homologous to sequences (homology arms) on either side of the targeted DNA break, and up to 4 kb of new DNA sequences between these homology arms. The cell's natural DNA repair process uses the homology arms to align the template in the correct location, and then copies and pastes the new DNA into the genome at the targeted gene cleavage site. This process enables correction or replacement of a mutated gene, or insertion of a new therapeutic gene in a precise location.

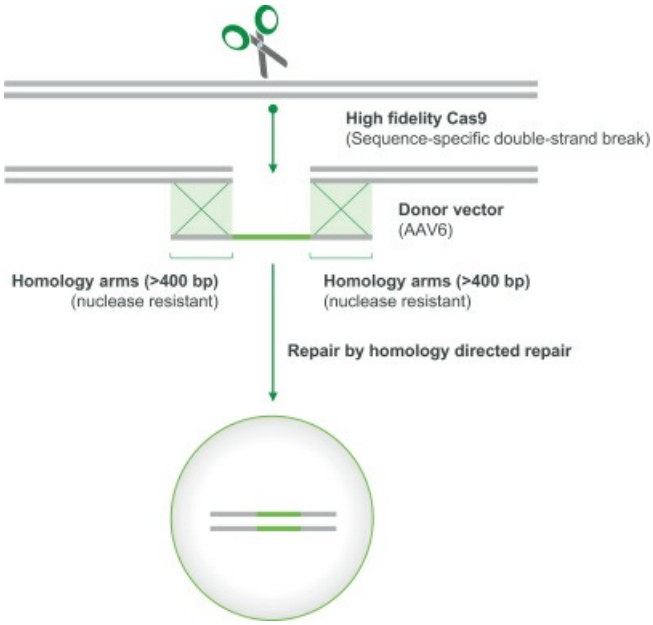


High Precision CRISPR-Based Nuclease

Our founders discovered that chemically modified guide RNAs can enhance Cas9 activity and subsequently showed that delivering Cas9 as a recombinant protein instead of as mRNA further increased cutting efficiency. These approaches are now widely used and widely considered to be state of the art for gene editing. We have continued to optimize the CRISPR component of our platform and employ an improved Cas9 enzyme with dramatically reduced off-target activity. We employ high fidelity Cas9, which was co-discovered by our founders, to reduce off target cutting by 20-fold on average and 30-fold on average for the SCD gene, thus providing potential improved safety. We believe this is a unique advantage for our programs.

Harnessing HDR

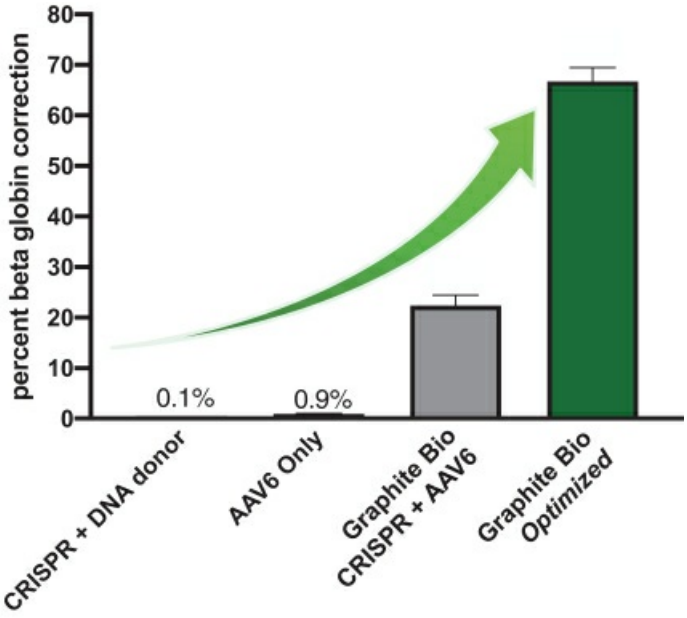
Cells naturally have the ability to repair their DNA if damaged. One highly specialized repair pathway is called HDR because the cell uses a homologous template to precisely "copy and paste" DNA sequences to repair a DNA break without introducing errors. Normally, the template used in HDR comes from the sister chromosome. Because of its precision and ability to use a template, harnessing the HDR pathway to achieve therapeutic targeted gene integration has been a long-sought but elusive goal due to its potential to dramatically expand gene editing's applications and curative potential.



To achieve "find & replace," as described above, we deliver an optimized, synthetic DNA template via a non-integrating AAV6 viral vector which is transduced into cells. Our founders evaluated various approaches before discovering that AAV6 achieved the most efficient transduction in comparison to nine other AAV serotypes, while optimally preserving stem cell function. Our AAV6 donor DNA template was iteratively optimized to maximize the efficiency of targeted gene integration. No viral genes are present in the template, and the template itself exists only transiently in the target cell population.

Process Optimization

HDR is most active during cell division and is inefficient in slowly dividing cells like HSCs. Achieving HDR at potentially curative efficiency in HSCs has been an elusive and highly-sought goal because HSCs are long-term multi-potent stem cells with broad therapeutic potential and potential lifetime durability. We believe this has now been achieved with the development of our platform. In our process, we use clinically validated and standard methods to isolate HSPCs from patients, which are comprised of both slowly dividing HSCs (lower rates of HDR) and more rapidly dividing progenitors (higher rates of HDR). Although edited HSPCs are the standard drug product for any gene edited autologous stem cell therapy, the therapeutic effect comes from the long-term HSCs that are a subset of the cells in the drug product. Harnessing our stem cell biology expertise, we optimized the timing of template delivery and cell culture conditions to improve gene correction frequency from approximately 20% in initial experiments to approximately 70% in human HSPCs in GPH101, our sickle cell program. We believe this gene correction rate in HSPCs ensures that the correction rate in the long-term stem cells can achieve the threshold required to cure patients (engraftment of 20% corrected cells).

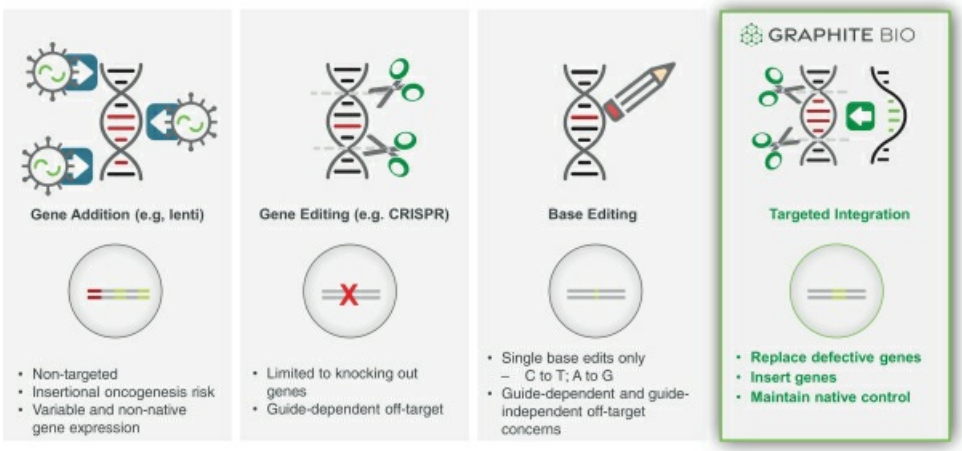


We believe our technology platform is revolutionary because it brings together proven individual technologies, new discoveries, and systematic process optimization to, for the first time, achieve HDR-mediated targeted gene integration at efficiencies of up to approximately 70% in human HSPCs. We have serially optimized our GMP process to retain high and potentially curative gene correction rates at clinical scale.

Our approach differs from first generation gene and base editing technologies:

- **Direct targeting and correction of genetic lesions:** We harness HDR to replace the disease-causing mutation or the entire disease-causing gene with the normal, wild-type genetic sequence. This is in contrast to first generation gene editing approaches that have focused on knocking-out or excising genes.

- **Efficiency of targeted gene integration:** In our GPH101 sickle cell gene correction program, we have demonstrated up to approximately 70% gene correction efficiency in HSPCs in *ex vivo* studies. In gene replacement and targeted gene insertion applications, we have consistently demonstrated efficiencies of approximately 30-50% in HSPCs across a range of gene targets and templates. We believe these efficiencies are above the curative threshold for a broad array of indications, including SCD. Prior to the development of our gene integration platform efficiencies using HDR in HSPCs were approximately 10%.
- **Breadth of applications:** We can replace genes of up to 4 kb allowing us to correct not only single point mutations but also multiple mutations within the same gene, and to address gene deletions. We can also precisely insert genes under control of a native promoter for naturally regulated expression, into a safe harbor location under the control of an exogenous promoter, or under the control of a lineage specific cellular promoter of choice.
- **Uniquely suited to expand the patient population eligible for potential one-time curative HSC therapies:** We believe that the high efficiency and precision of our targeted gene integration platform can reduce threshold bone marrow engraftment levels. This could potentially obviate the need for full chemotherapeutic myeloablative bone marrow conditioning (the current standard for allo-HSCT and most gene editing and gene therapy approaches in development). In addition, our approach avoids the theoretical risk of insertional oncogenesis from integrating viral vectors and incorporates a high fidelity CRISPR-based nuclease, for potentially improved safety. Pairing these advantages with targeted and safer bone marrow conditioning could bring HSC-based curative therapies to much larger numbers of patients.



Key Differentiated Components of Our Technology Platform

Our platform combines two powerful, well characterized biologic approaches—CRISPR and HDR—with our HSC expertise and know-how to achieve high efficiency targeted gene integration.

Efficient cutting with a CRISPR-based nuclease is an important first step in our process. Our founders discovered that chemically modified guide RNAs can enhance Cas9 activity and subsequently showed that delivering Cas9 as a recombinant protein instead of as mRNA further increased cutting efficiency. These approaches are now widely used and widely considered to be state of the art for gene editing. We have continued

to optimize the CRISPR component of our platform as described below together with additional differentiated and proprietary components our technology and process:

- **Use of HiFi Cas9 to reduce off-target DNA cleavage**. One of the concerns about CRISPR-based nuclease gene targeting systems is unintended cleavage at other sites that may closely match but are not identical to the sequence targeted by the guide RNA. As shown in the figure below, we observed in our preclinical studies that a Cas9 variant, known as HiFi Cas9, can reduce off-target DNA cleavage by as much as 20-fold on average and 30-fold on average for the SCD gene with no meaningful change in the rate of on-target cleavage. We believe that this increased precision is one of the factors that could increase the safety and overall benefit/risk profile of our targeted gene integration therapies, potentially expanding patient eligibility and potential indications for our product candidates.

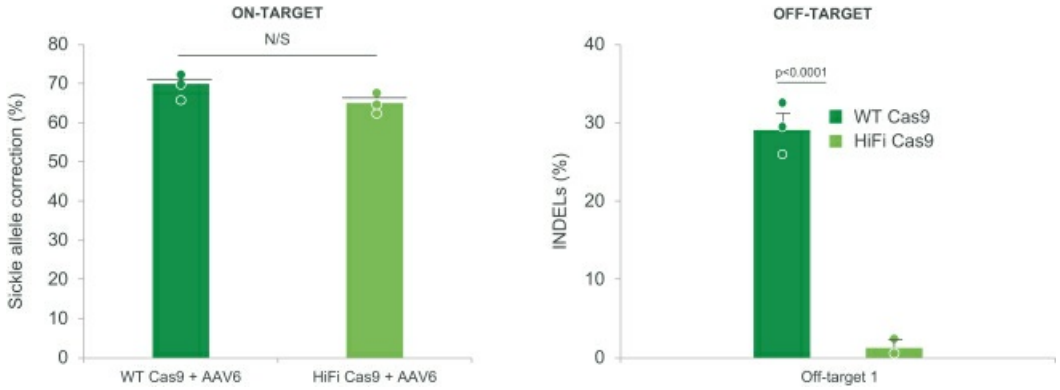


Figure: HiFi Cas9 had an approximately thirty-fold reduction in off-target DNA cleavage compared to wild-type Cas9.

- **Use of AAV6 to deliver DNA template**. To harness HDR, we deliver a DNA template via a non-integrating AAV6 viral vector which is transduced into cells. Our founders evaluated various AAV serotypes before discovering that AAV6 achieved the most efficient transduction, or the transfer of genetic material into a cell.

To determine relative transduction efficiencies across AAV serotypes, human primary hematopoietic progenitors were infected with ten AAV serotypes each carrying the green fluorescence protein (GFP) reporter gene. The experiment was designed to determine relative transduction efficiency rather than to maximize transduction. As shown in the figure below, we observed that AAV6 was most efficient in comparison to nine other AAV serotypes. Our founders later discovered that additional optimization and ribonucleoprotein (RNP) electroporation prior to AAV6 transduction further enhanced AAV transduction efficiency.

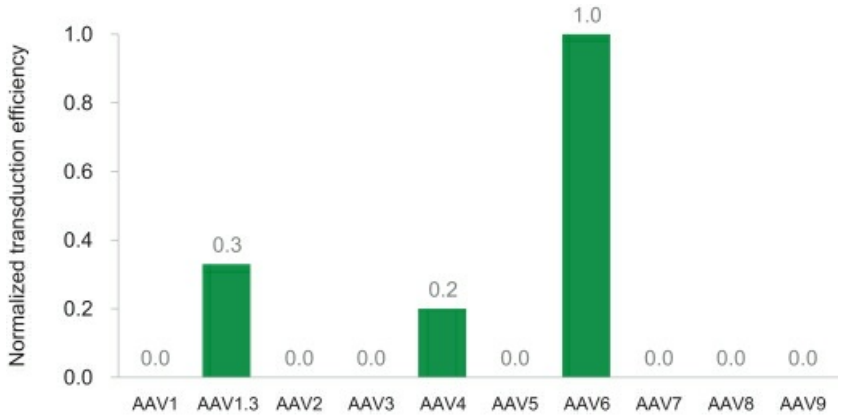


Figure: AAV transduction of human primary hematopoietic progenitor cells.

- **Ability to achieve high rates of gene integration in a wide range of therapeutic cell types, including HSCs** HDR is a cellular process that is primarily active during cell replication and, for this reason, slowly dividing cells like HSCs have been historically recalcitrant to HDR based gene editing. We have shown that stimulating cell replication with growth factors, reducing cell density and other factors can increase the proportion of cells that undergo HDR and site-specific gene integration. As shown in the figure below (left), we observed that HSCs which are pre-stimulated with cytokines and subsequently cycled four times achieve approximately twice the rate of gene integration. As shown in the figure below (right), HSCs plated at 10-fold less density achieved nearly twice the rate of gene integration. We believe that this optimization is crucial to inducing the conditions that significantly favor the repair of CRISPR-Cas9-driven DNA break by HDR.

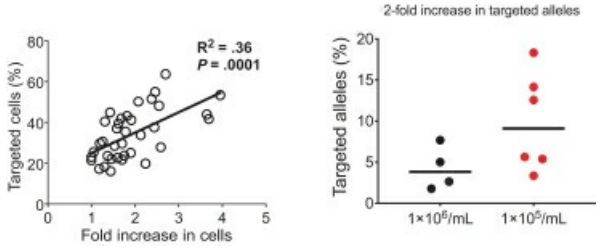


Figure: Optimization of HSC cell culture conditions led to an increase in the rate of homologous repair and gene insertion.

We have found that each of these optimization steps and our other know-how can contribute to the creation of a highly efficient targeted gene integration process. We have further optimized our process to maintain high levels of efficiency at clinical scale using HSPCs isolated from healthy donors.

Expanding Eligible Patients and Potential Indications: Combining Our High Efficiency Approach with Advances in Non-Genotoxic HSC Targeted Conditioning

The high precision and high efficiency with which we can consistently introduce genes by HDR has the potential to greatly expand the application to more patients and the types of diseases for which gene editing based therapies are feasible.

A limitation of therapies based on *ex vivo* genetic manipulation of HSCs is that the patient must be pre-conditioned with non-targeted, genotoxic conditioning agents, to both eliminate the dysfunctional endogenous HSCs and to create room for the modified cells to engraft and expand. This approach is standard for allogeneic bone marrow transplant (e.g., for SCD) and for approved HSC gene therapy products and has safety risks such as transient neutropenia, which necessitates prolonged hospitalization, potential fertility impairment, and the risk of secondary malignancies. These risks may reserve use of *ex vivo* HSC-based genetic and potentially curative therapies for diseases with limited treatment options, and for the most severely affected patients.

We believe that our ability to generate HSC-based product candidates that contain a high percentage of corrected cells may reduce the need for chemotherapy-based myeloablation by allowing use of non-genotoxic HSC targeted conditioning regimens. This potential advance, as well as harnessing precision gene insertion and using a higher fidelity CRISPR-based nuclease may further enhance safety and could ultimately expand the types of diseases and patients who could be treated safely and potentially cured with our product candidates.

For our XSCID program, we intend to incorporate non-genotoxic HSC targeted antibody conditioning. As we generate additional preclinical and clinical data, we anticipate using non-genotoxic HSC targeted conditioning regimens to expand the application of our product candidates to additional patients and indications. Because XSCID treatment is anticipated to require only 5% engraftment of corrected cells, it is the most likely of our programs to be able to combined with a non-genotoxic HSC targeted antibody conditioning regimen. The figure below shows the fold difference for corrected engrafted cells over the curative threshold for our three development programs. Higher fold differences indicate that non-genotoxic HSC-targeted conditioning is more likely to be effective.

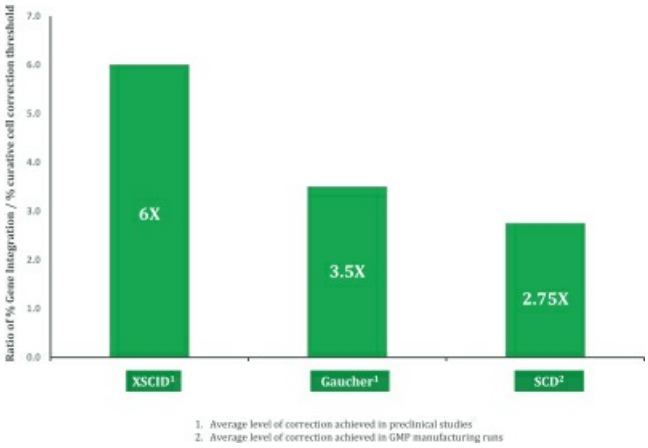
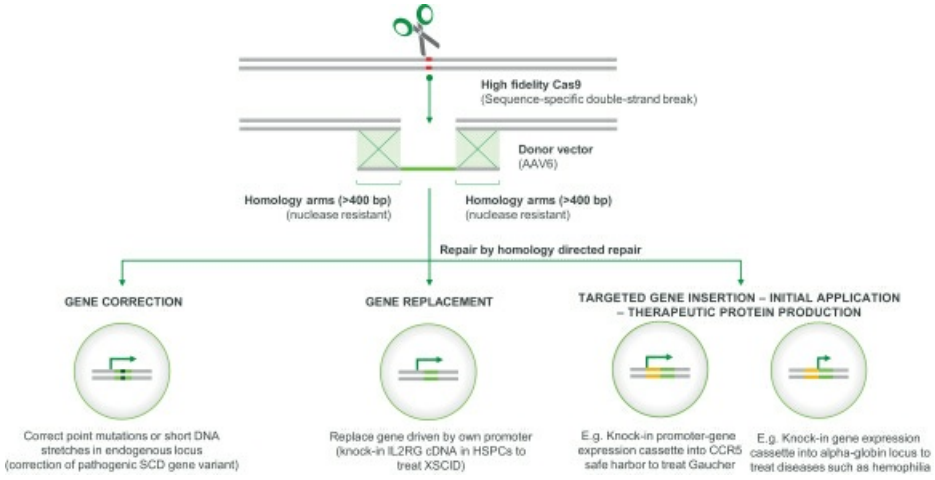


Figure: Multiple of gene correction achieved over curative engraftment threshold. Higher multiples may require lower potency conditioning

Applications Enabled by Our Technology

We are applying our next generation gene editing platform in three settings: gene correction, gene replacement and targeted gene insertion.

- **Gene Correction:** Fix an existing gene by directly correcting the specific mutation in a dysfunctional gene.
- **Gene Replacement:** Replace dysfunctional genes with a new normal copy of an entire gene at their location in the chromosome.
- **Targeted Gene Insertion:** Targeted insertion of entire gene cassettes into chosen chromosomal locations initially applied to drive permanent production of therapeutic proteins.



Our Product Candidates

Gene Correction: GPH101 for the Treatment of SCD

Overview of GPH101

Our lead product candidate, GPH101, is a next generation gene-edited autologous HSC product candidate that is designed to directly correct the mutation responsible for SCD. The mortality and morbidity associated with SCD, all caused by a single mutation, has made curing SCD by direct gene correction a dream of many clinicians. Indeed multiple genetic therapies are in development to address SCD, but due to technical limitations of other approaches, these therapies are primarily focused on expressing alternate hemoglobin genes such as fetal hemoglobin or a transgenic hemoglobin. Our approach is the first in industry to directly correct the SCD-causing mutation to restore normal adult hemoglobin expression. We have received clearance of our IND and intend to enroll the first patient in a Phase 1/2 trial of GPH101 in .

Overview of Sickle Cell Disease

SCD is caused by a single nucleotide substitution in the gene encoding the ß subunit of hemoglobin (Hb), resulting in the production of Hemoglobin S (HgbS). SCD is an autosomal recessive disease, meaning individuals with SCD have two copies of the mutated ß globin gene. HgbS polymerizes in red blood cells to form rigid rod-like structures, damaging cell membranes and causing red blood cells to take on a characteristic sickle shape ultimately resulting in hemolytic anemia (destruction of red blood cells) and vaso-occlusion (blockages in blood

vessels), the two major pathophysiologic features of SCD. The anemia and vaso-occlusion cause severe symptoms, serious morbidity including multiple organ damage, and shortened lifespan.

SCD is the most common monogenic disorder with an estimated global incidence of over 300,000 births annually. Population estimates suggest that there are approximately 100,000 persons living with SCD in the United States with an additional 67,000 people living with the disease in the European Union. The global prevalence of the disease is estimated to be about 20-25 million. Unaffected biological parents of individuals with SCD have sickle cell trait. Sickle cell trait is the benign carrier status (one copy of normal and one copy of mutated ß globin) of SCD present in over 100 million people worldwide.

SCD is a serious and life-threatening disease. Quality of life is often poor and life expectancy is reduced by20-30 years. Patients experience severe, often daily symptoms of pain and fatigue, suffer from acute painful episodes often requiring hospitalization, and are at risk for serious complications and organ damage including stroke, silent cerebral infarction, osteonecrosis, renal failure, pulmonary hypertension and cardiomyopathy.

Sickle Cell Disease—Available Treatments and Unmet Needs

There are four available therapies approved by the FDA SCD treatment: hydroxyurea, L-glutamine, and Adakveo™ (crizanlizumab) to reduce the frequency of vaso-occlusive crises (VOCs), and Oxbryta™ (voxelotor) to increase hemoglobin levels and reduce hemolysis. These therapies require lifelong usage and may in some cases reduce but do not eliminate SCD's serious symptoms or complications. None of these therapies has been shown to prevent pain or, organ damage, or to increase survival. Chronic blood transfusion therapy is another treatment option for some SCD patients. While transfusion therapy has a role in decreasing risk of stroke, a dreaded SCD complication, it has significant side effects including iron overload. Despite advancements in current care, progressive organ damage continues to cause early mortality and severe morbidity.

Allo-HSCT remains the only curative therapy for SCD and is considered the gold-standard for potentially curative therapies. The HSCT procedure ablates the patient's endogenous HSCs that produce sickle red blood cells and replaces them with normal HSCs, typically from a matched sibling donor with sickle trait. HSCT is considered curative because donor cells contain at least one corrected copy of the beta globin gene and produce normal adult Hb (HgbA) yielding normal red blood cells thereby preventing disease complications . HSCT with donor sickle trait cells has been shown to be curative because every red blood cell contains approximately 60% HgbA protein and 40% HgbS protein and does not sickle. HSCT is the only therapy for SCD proven to prevent progression of organ damage and prolong survival. However, HSCT is rarely used due to the difficulty in finding a matched donor (as low as 16-19%), safety risks, including graft-versus-host-disease, and need for long-term immunosuppression.

Despite HSCT's limitations, over 150 are performed in the United States annually. We believe this indicates substantial underlying demand for curative options which is driven by SCD's severity and inadequacy of current treatment options.

Sickle Cell Disease—Emerging Curative Treatments and Potential Limitations

Gene therapy and gene editing approaches are attractive alternatives to HSCT because a patient's own cells (autologous cells) are genetically modified and therefore do not face the high risk of rejection or graft-versus-host disease associated with allo-HSCTs. However, it is unclear whether gene therapy (gene addition) and gene editing (hemoglobin F (HgbF) induction) approaches currently in the clinic can achieve long term benefits similar to allo-HSCT, which directly replaces stem cells with HbSS genotype with normal (HbAA) or sickle trait (HbAS) stem cells from a matched sibling donor.

Gene addition approaches coopt a LVV to semi-randomly integrate a modified gene fornon-sickling beta (or gamma) hemoglobin into the genome, leaving the disease causing sickle globin gene intact. Results from

these trials are promising and demonstrate that patients treated using this approach have reduced VOC incidence, significant hemoglobin increases and reduction in hemolysis. However, the random insertion of newly introduced genes raises safety concerns for a potential increased risk of tumorigenesis. Use of viruses such as LVV to insert genes also results in a high variability in the number of gene copies that are inserted into the genome. This leads to variable expression levels of transgenic hemoglobin such that a significant proportion of red blood cells may not be protected. Finally, LVVs have a biologic preference for integrating into the introns of actively expressed genes which might cause long-term perturbations of HSC function that might take years to manifest themselves.

A different, yet indirect, approach uses CRISPR-Cas9 gene editing to reduce or eliminate the suppression of fetal hemoglobin expression thereby increasing the fetal hemoglobin levels. As with LVV gene addition, this approach also leaves the disease-causing sickle mutation intact. The rationale for this approach is that rare patients with naturally occurring elevated fetal hemoglobin levels may have reduced or minimal SCD symptoms. Data available on three treated patients suggests that this fetal hemoglobin induction also reduces the rate of VOCs and results in significant hemoglobin increases and reduction in hemolysis. Fetal hemoglobin serves to transfer oxygen from the maternal blood stream to the fetus because it has a higher oxygen affinity compared to adult hemoglobin. Fetal hemoglobin is normally expressed only in the fetus and replaced by adult hemoglobin within one year of birth. Due to its abnormally elevated oxygen affinity for adults, prolonged elevated fetal hemoglobin expression may result in adverse physiological consequences.

Therefore, we believe that current gene editing and gene addition approaches, while promising, stop short of correcting the underlying disease-causing mutation, which remains the ultimate goal of an SCD curative therapy.

Our Solution: GPH101

GPH101 is the first targeted genetic therapy that is designed to efficiently and precisely correct the disease-causing gene, simultaneously eliminating sickle hemoglobin and restoring normal adult hemoglobin expression. At the DNA level, we believe this is the first approach in the industry that seeks to convert a SCD genotype (two genes with sickle mutations, HbSS) to a normal genotype (at least one normal ß globin gene). By correcting the SCD causing mutation, our next-generation gene editing approach overcomes a major limitation of current gene addition and gene editing approaches that take an indirect approach. Our goal with GPH101 is to replace a sufficient quantity of a patient's HSCs with gene corrected cells to definitively cure SCD.

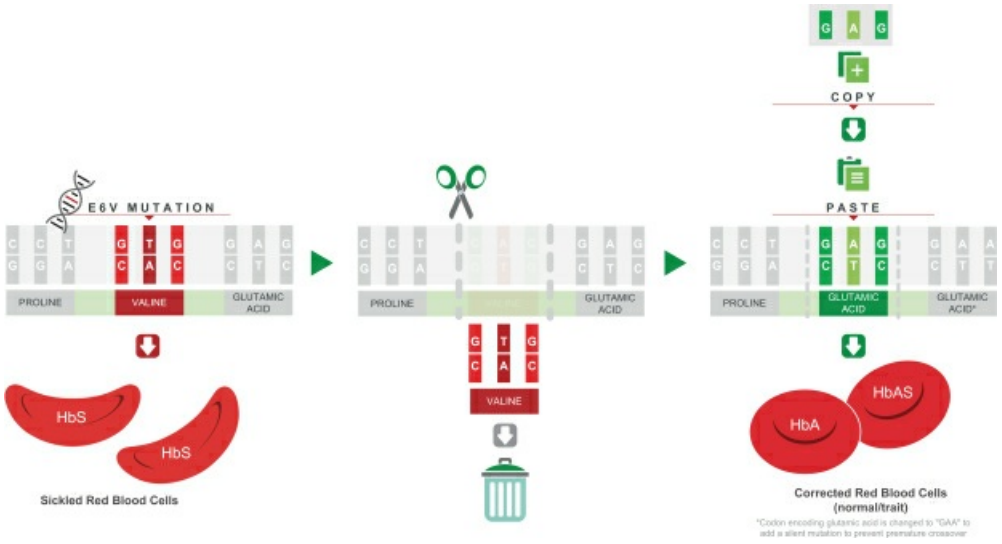


Figure: GPH101 is removes the mutated region of HbS and replaces it with that of a normal hemoglobin gene.

In order for this approach to be curative in patients, it is not necessary to correct all sickle globin genes nor to correct all HSPCs. Because sickle cell trait individuals have benign SCD carrier status, correcting one out of the two sickle globin genes in a cell is sufficient to correct that cell. Furthermore, to cure the disease, it is not necessary to correct all SCD HSPCs. In patients who received allo-HSCT from a matched sibling donor with sickle trait—long-term, persistent mixed donor chimerism where only 20% of HSCs have normal hemoglobin resulted in cures, and clinical benefits were observed with as low as 5% corrected cells. Per the figure below, we have shown under IND-enabling GMP manufacturing conditions that we can achieve correction (meaning one or more corrected copies of the sickle globin gene) in 55% of HSPCs, which we believe to be well above the curative threshold.

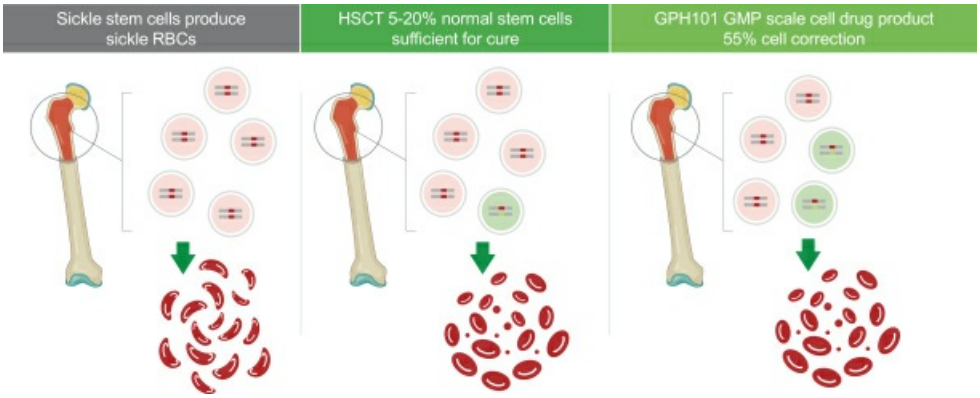


Figure: We have shown that under IND-enabling GMP manufacturing conditions that we can achieve HbS gene correction above the threshold required for cure.

We believe that GPH101 has the potential to be the optimal curative approach, because it is designed to directly correct the mutation responsible for SCD and restore normal biology by eliminating sickle globin and restoring adult hemoglobin expression.

Preclinical Validation

We have taken two experimental approaches to generate preclinical proof of concept data for GPH101. The first approach corrects the HbS gene in HSPCs isolated from patients, then measures the function of treated cells both *ex vivo* and in a humanized mouse model. The second approach corrects the HbS mutation in HSCs from a sickle mouse model and assesses corrected cells' ability to modify the disease.

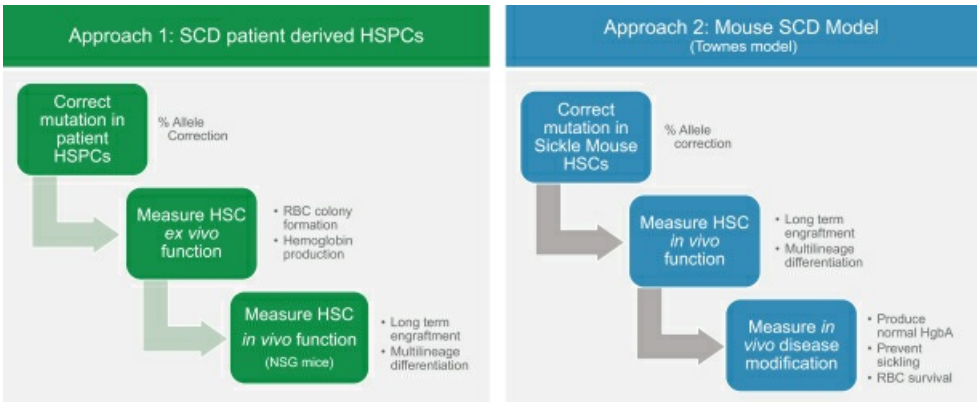


Figure: Two experimental approaches were used to generate proof-of-concept data for GPH101 in preclinical models

SCD Patient Derived HSPCs

In experimental approach 1, HSPCs were isolated from SCD patients and edited utilizing a process similar to the intended process for clinical samples, as illustrated below in the left panel of figure below. Due to our optimized process, over 60% of HbS alleles were corrected, approximately 20% had INDELs and only approximately 10% of HbS alleles remained intact. We believe that the INDELs may be beneficial to SCD patients since INDELs prevent expression of sickle hemoglobin from the uncorrected intact HbS genes.

Next, these edited HSPCs were differentiated into red blood cells *ex vivo* and their hemoglobin expression was measured. As illustrated in the middle panel of the figure below, analysis of HgbA and HgbS expression (subtracting background HgbF levels) showed over 90% normal hemoglobin A and only approximately 10% sickle hemoglobin. We believe this result was better than expected for sickle trait, where red blood cells contain 60% HgbA protein and 40% HgbS protein, because INDEL formation in uncorrected sickle alleles eliminated most HbS expression. As illustrated in the right panel of the figure below, when transplanted into immunodepleted NSG mice, these cells engrafted in a long-term (16 weeks), stable fashion with approximately 30% of sickle alleles corrected. This translates into approximately 40% of the long-term HSCs being corrected by containing at least one corrected sickle allele, double the expected curative threshold in humans. We can measure corrected alleles more directly than corrected cells; the curative threshold based on corrected alleles is anticipated to be approximately 15% because the percent of cells that have at least one corrected allele is approximately 1.3 times higher than the percent of corrected alleles. Possible reasons for the approximately two-fold difference in gene correction between the infused HSPCs (approximately 70%) and the HSCs engrafted in the mice (approximately 35%) include that long term engrafting HSCs have lower efficiency HDR than progenitor cells that comprise the majority of HSPCs; that this is a feature specific to the mouse model; or that

the gene correction process impairs functionality of some of the HSCs. Regardless of the explanation, the 30% gene correction seen *in vivo* in engrafting HSCs is predicted to be curative in humans.

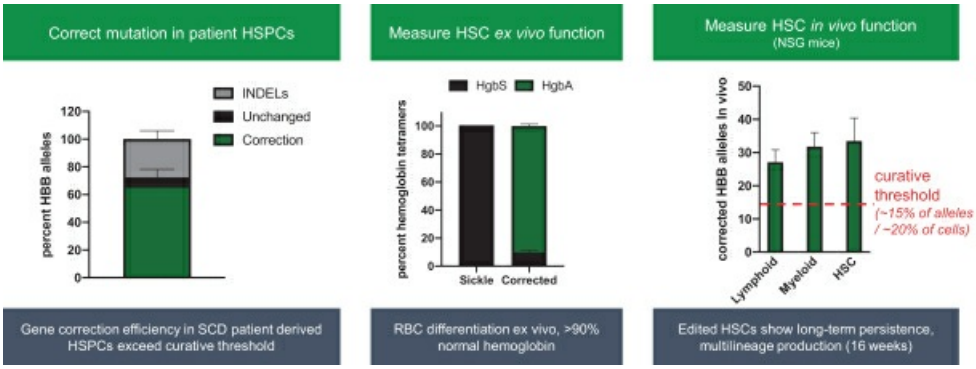


Figure: GPH101 created from SCD patients predominantly expressed normal hemoglobin and led to stable engraftment in immunodeficient mice

Mouse SCD Model (Townes Model)

The Townes model of SCD is a transgenic mouse model in which the mouse hemoglobin locus is replaced with human HbA and HbS genes. These mice express sickle cell hemoglobin and exhibit many of the symptoms of human SCD including red blood cell sickling and short red blood cell half-life. In this experimental approach HSCs were isolated from sickle mice and edited utilizing the same process as the process for human HSPCs. As illustrated in the left panel of the figure below, we observed that approximately 20% of sickle alleles were corrected in the mouse HSCs, likely because of processes that were optimized for human and not mouse HSCs. Given the curative threshold in humans of 20% HSCs, we predicted that mice achieving 20% or greater correction of engrafted cells (15% of alleles) would show substantial benefit of disease features. As illustrated in the center panel of the figure below, all mice with greater than 15% allele correction showed a profile of hemoglobin expression consistent with a potential cure with over 60% HgbA protein (same HbA level as sickle trait). Furthermore, red blood cells from gene-corrected mice had a half-life that was approximately ten-fold longer than SCD mice. As illustrated in the right panel of the figure below, we observed that these gene-corrected red blood cells were resistant to sickling.

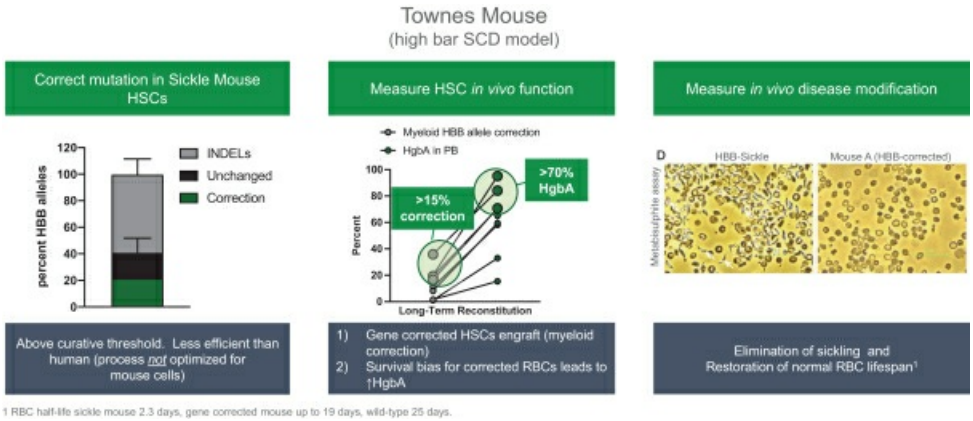


Figure: Gene correction in a humanized SCD mouse model resulted in over 70% normal hemoglobin expression leading to reduced red blood cell sickling.

GPH101 Phase 1/2 Clinical Trial Design

We received IND clearance for GPH101 and intend to initiate a Phase 1/2 open label clinical trial of GPH101 in approximately 15 patients with severe SCD in . The objectives of this trial will be to assess safety, engraftment success, gene correction rates, total hemoglobin, hemoglobin A and S, and clinical and exploratory endpoints.

Gene Replacement: GPH201 for the Treatment of XSCID

Our GPH201 product candidate is a next generation gene-edited autologous HSC product candidate for the treatment of XSCID. XSCID is a rare, life-threatening disease where multiple mutations in a single gene prevent the formation of multiple interleukin receptors resulting in defects in immune cell formation. GPH201 replaces this gene with a normal copy, conferring a survival advantage to treated cells. We have an agreement to investigate the potential use of a clinical-stage non-genotoxic HSC targeted antibody-based bone-marrow conditioning (non-genotoxic HSC targeted conditioning) regimen with GPH201.

XSCID Disease Overview and Unmet Need

XSCID is the most common type of a group of severe primary immunodeficiency disorders characterized by developmental and/or functional impairment of lymphocytes. XSCID accounts for about 40%-50% of all SCID cases in United States and with an estimated prevalence of 1 in 100,000 live births and almost exclusively affects males. The IL2RG gene encodes the interleukin 2 receptor gamma subunit, an essential component of a number of cytokine receptors required for normal lymphopoiesis. Because of multiple mutations in the IL2RG gene in XSCID patients, B-, T- and NK-cells either fail to develop and proliferate due to the inability to respond to mitogenic stimuli. T and NK-cells normally play a critical role in protection from infection with pathogens such as bacteria, viruses, and fungi. As a consequence, severe, persistent, or recurrent early-onset infections are the hallmark of XSCID. Without treatment, infants with XSCID usually do not live beyond one year of age.

Allogeneic HSCT that results in functional reconstitution of the immune system is the only curative treatment for XSCID. Allogeneic HSCT, performed in the first 3.5 months of life, using human leukocytes antigen (HLA)-matched sibling donors results in over 94% chance of long-term, disease-free survival. While the results of allogeneic HSCT can be excellent, the procedure has limitations including identification of an HLA matched sibling donor as well as potential complications of GvHD and subsequent poor immune reconstitution.

To date, almost 200 unique mutations in the IL2RG gene have been identified in more than 320 patients with X-SCID. This diversity of IL2RG mutations that can cause XSCID makes developing genetic therapies for XSCID challenging. An effective targeted genetic therapy would need to replace a large portion of the IL2RG gene in order to be effective across XSCID patients with different IL2RG mutations.

XSCID was among the first indications pursued for genetic medicine development. Although gene therapy has shown promising results, early clinical trials using gamma retroviral vectors to insert extra IL2RG gene copies led to insertional mutagenesis and leukemia in a significant proportion of patients. Subsequently, LVV for IL2RG gene addition have entered development. LVV has decreased insertional mutagenesis risk, but potential risk remains. Furthermore, LVV gene addition in XSCID may lead to suboptimal immune reconstitution due to constitutive unregulated transgene expression.

Our Solution: GPH201

GPH201 is a therapy for XSCID in which the defective IL2RG gene is replaced in autologous HSCs at its natural locus in the genome with a normal IL2RG gene. The goal of GPH201 is to replace a sufficient quantity of a patient's HSCs with gene edited cells to eliminate the symptoms of, and potentially cure, XSCID.

Preclinical Data

To assess gene replacement efficiency, we modified HSCs from healthy males using our GPH201 process. As illustrated in the figures below, we observed an overall mean IL2RG gene replacement efficiency of approximately 45% in healthy donor-derived HSPCs. These HSCs were then engrafted in bone marrow of immunodeficient mice where approximately 30% gene replacement was observed, indicative of long-term curative potential. We believe this level of gene replacement is well in excess of the 1-5% curative threshold.

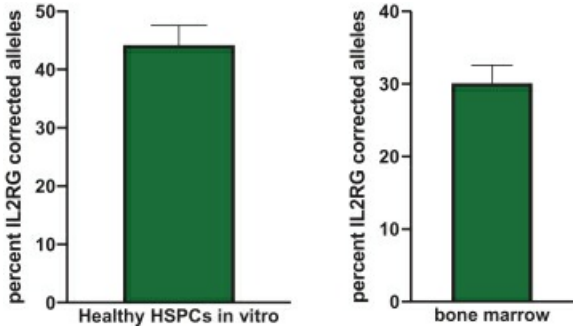


Figure: The IL2RG gene was replaced in approximately 45% of treated HSPC cells from healthy donors

To assess the potential of our treatment to restore the ability of progenitor cells to differentiate into T cells and NK cells, we isolated HSPCs from a XSCID patient with subsequent replacement of the IL2RG gene, achieving approximately 40% gene replacement efficiency. Upon differentiating these cells *in vitro,* as illustrated in the figure below, treated HSPCs from the XSCID patient had significantly larger percent of cells that formed T cells and NK cells than untreated control cells.

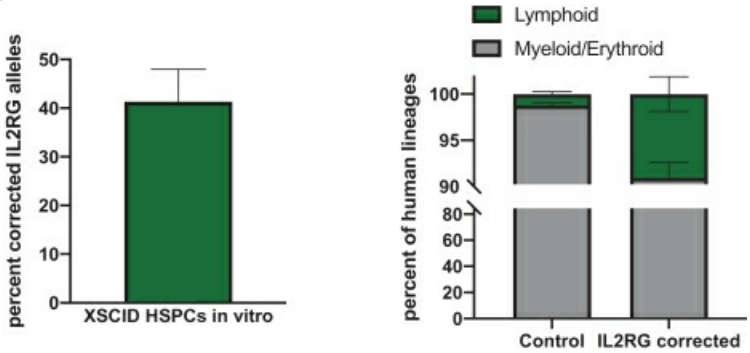


Figure: IL2RG gene replacement in XSCID patient HSPCs led to significant increase in T cell and NK cell formation

As a result of the selective advantage of progenitor and effector cells that express normal IL2RG, it is estimated that onlyl-5% of genetically corrected HSCs would be needed to reconstitute immunity in XSCID patients. This selective advantage is highlighted by reports that rare XSCID patients have had a somatic reversion in a single precursor cell that led to reconstitution of their immune system for years. Based on the editing efficiency we have demonstrated and the low number of genetically corrected HSCs needed to potentially cure the disease, we believe that GPH201 can be curative and could be combined with a novel, safer and targeted bone marrow conditioning approach.

We have partnered with Jasper Therapeutics to assess GPH201 combined with targeted conditioning using JSP191, an anti-CD117 monoclonal antibody and without the use of chemotherapeutic myeloablation. Clinical data has shown that JSP191 can lead to successful engraftment in allo-HSCT for XSCID.

GPH201 Phase 1/2 Clinical Trial Design

We intend to conduct a Phase 1/2, multicenter, open-label trial to assess the safety, efficacy and pharmacodynamics of GPH201 combined with a non-genotoxic HSC targeted conditioning regimen in patients with XSCID who have no matching sibling donor.

We believe that GPH201 will generate preliminary data on combining our autologous HSC therapies withnon-genotoxic HSC targeted conditioning, and that our clinical experience with this approach with GPH201 will accelerate our ability to use a potential non-genotoxic HSC targeted conditioning regimen with our other product candidates in our pipeline. We believe GPH201 will serve as proof of concept for our platform's ability to achieve native gene replacement, an approach that can potentially be applied to many other diseases such as B-thalassemia, other immunodeficiencies, and autoinflammatory syndromes.

Targeted Gene Insertion with Therapeutic Protein Production (CCR5 Safe Harbor Locus): GPH301 for the Treatment of Gaucher Disease

Our GPH301 product candidate is a next generation gene-edited autologous HSC product candidate from our CCR5 locus technology for the treatment of Gaucher disease. With GPH301, we are inserting a functional copy of the gene for glucocerebrosidase (GCase) into the chromosomal location of the CCR5 gene. This locus is known as a safe harbor both because of the lack of serious deleterious effects in humans with CCR5 mutations and because the expression of genes inserted there can be precisely controlled by regulatory elements inserted together with the gene of interest. We intend to develop GPH301 for the treatment of both Type 1 and Type 3 Gaucher disease. For the more serious Type 3 disease, we anticipate using standard chemotherapy-based conditioning; for Type 1 we will explore targeted conditioning regimens. This same approach can be used for production of therapeutic proteins for other diseases including other lysosomal storage diseases. We believe that proof of concept in Gaucher can accelerate development of a pipeline of CCR5 safe harbor protein production candidates.

Overview of Gaucher Disease

Gaucher disease is an autosomal recessive genetic disorder caused by mutations in the GBA gene which encodes GCase. GCase is an enzyme responsible for degrading glucocerebroside, a cell membrane building block, into glucose and lipids within lysosomes of cells. In patients with Gaucher disease, lack of GCase leads to accumulation of glucocerebroside in macrophages resulting in inflammation that impacts the liver, spleen and bone marrow.

Gaucher disease is classified into three types. Type 1 disease is associated with hematologic abnormalities, enlargement of the liver and spleen and skeletal defects. While patients with Type 1 disease typically have normal lifespans, their quality of life is severely impacted. Patients with Type 2 disease develop life-threatening neurological dysfunction as infants and often die within the first few weeks of life. Type 2 disease is typically too rapidly progressive for HSCT treatment. Patients with Type 3 have severe neurological complications in addition to all the symptoms associated with Type 1 disease. Patients with Type 3 disease have a reduced lifespan, but can often survive into young adulthood.

Gaucher disease is the most common inherited lysosomal storage disease. There are approximately 6,000 patients with Gaucher disease in the United States. 90% of Gaucher patients in the United States and Europe are classified as Type 1. Type 3 disease may be the most common type worldwide.

Gaucher Disease—Standard of Care Treatments

Gaucher disease is currently treated by enzyme replacement therapy (ERT), which is recombinant GCase. All of the approved ERTs are administered as biweekly infusions. Long term ERT for Gaucher disease results in lower levels of anemia, reduced bone pain, and reductions in spleen and liver enlargement but are not curative. An unmet need exists for Type 1 patients despite ERT, with 60% of patients achieving suboptimal clinical outcomes after 4 or more years of treatment. A clinically significant percentage of patients continue to exhibit bone pain, organomegaly and cytopenia after 10 years of ERT.

Since ERTs cannot cross the blood brain barrier, they are ineffective in addressing the neuropathic manifestation of the disease in Type 2 and Type 3 patients. HSCT is the only treatment that can provide a definitive cure for Gaucher disease and is considered prior to the onset of neurologic symptoms.

An alternate method of treating Gaucher disease is to block the synthesis of glucocerebroside with inhibitors rather than to accelerate its breakdown with ERT. Approved products in this category include miglustat and eliglustat. These products are not generally as effective as ERT and have significant safety risks.

Our Solution: GPH301

GPH301 is targeted gene insertion therapy for the treatment of Gaucher disease in which a functional copy of the GBA gene is inserted into the CCR5 gene locus of autologous HSCs. This locus is known as a safe harbor both because of the lack of deleterious effects associated with gene insertions that occur there and because the expression of genes inserted there can be precisely controlled by regulatory elements inserted together with the gene of interest. We include the CD68S promoter in the inserted gene cassette which we believe provides two advantages: 1) targeting GCase expression specifically to the disease-causing cell in Gaucher (and avoiding expression in HSCs which could affect stem cell function) and 2) macrophage expression takes advantage of the ability of gene corrected macrophages to cross the blood brain barrier and address the neuropathic manifestation of Type 3 Gaucher Disease. The goal of GPH301 is to replace a sufficient quantity of a patient's HSCs with gene edited cells to drive GCase expression in a patient's macrophages and reverse the accumulation of unprocessed glucocerebroside. Data from Gaucher patients with mixed donor chimerism and from mouse models support that less than 10% corrected HSCs could be curative.

Preclinical Data

To assess the efficiency of our targeted gene insertion process, we isolated HSCs from healthy donors using our GPH301 process. As illustrated in the left panel of the figure below, we were able to achieve efficient gene insertion as demonstrated by approximately 35% of the targeted CCR5 alleles containing a GCase insertion. As illustrated in the center panel of the figure below, the edited, engrafted cells contain more than 10% alleles with the insertion, which corresponds to more than 15% of the cells, which is above the predicted threshold (5%-10%) for patients to achieve a cure. As predicted, because of our use of the CD68S promoter, GCase expression was restricted to monocytes and macrophages. As illustrated in the right panel of the figure below, GCase expression was two-fold higher in edited versus unedited healthy donor cells in both*in vitro* cultures and in cells isolated from a humanized mouse model after engraftment. We believe that this preclinical data strongly supports the curative potential of GPH301.

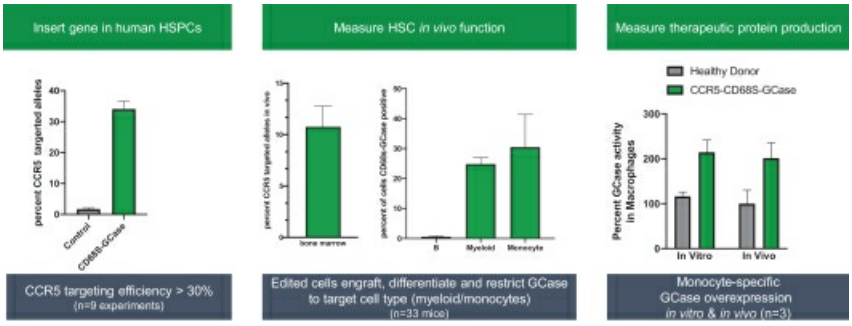


Figure: Insertion of the GBA gene in the CCR5 safe harbor led to the expression of GCase in monocytes.

GPH301 Planned Phase 1/2 Clinical Trial

We intend to conduct a Phase 1/2, multicenter, open-label trial to assess safety, preliminary efficacy and pharmacodynamics of GPH301 initially using standard busulfan conditioning in Type 1 and Type 3 patients and then explore the use of non-genotoxic HSC targeted conditioning regimen in Type 1 Gaucher disease patients.

Future Targeted Gene Insertion with Therapeutic Protein Production (CCR5 Safe Harbor) Opportunities

We plan to pursue indications beyond Gaucher disease using our CCR5 locus technology for tissue-based protein expression, including for CNS protein delivery. Inserting different genes into this locus using the same sgRNA, integration site and homology arms enables us to rapidly expand into other diseases, a number for which we have published animal or *in vitro* data.

Future Opportunities in Targeted Gene Insertion with Therapeutic Protein Production: Alpha Globin Locus

For certain therapeutic applications, we believe there is an advantage to precisely inserting a gene into a location in the chromosome where we can utilize a native cell promoter that can lead to high level and lineage specific expression. One such locus is the alpha globin locus, in which the endogenous alpha-globin promoter can be used to express inserted genes in red blood cells or red blood cell precursors to drive therapeutic protein production. This is an attractive approach because the very high rate of red blood cell formation (200 billion produced each day), coupled with the strength of the alpha globin promoter (280 million hemoglobin molecules per red cell) could allow for production of normal levels of therapeutic protein with modest HSC engraftment targets (<10%) which may be achievable with non-genotoxic HSC targeted bone marrow conditioning regimens. We believe this could dramatically improve the benefit risk of product candidates as potential one-time HSC cures.

A number of blood diseases including hemophilias, thalassemias and other diseases such as hereditary angioedema (HAE) and alpha-1 antitrypsin (AAT) deficiency could potentially be cured or treated by one time infusion of HSPCs with targeted gene insertion into the alpha globin locus. In preclinical studies, we observed a targeted insertion of a cDNA into this locus led to an approximately 40% gene insertion rate in human HSCs. Following the insertion, transplantation of these cells into a humanized mouse model resulted in long-term engraftment and gene expression.

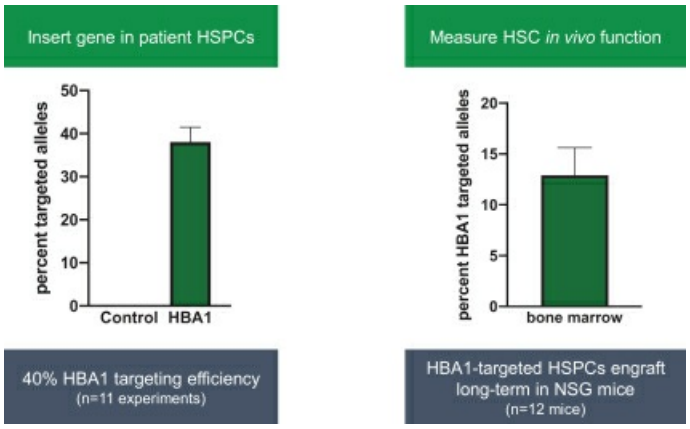
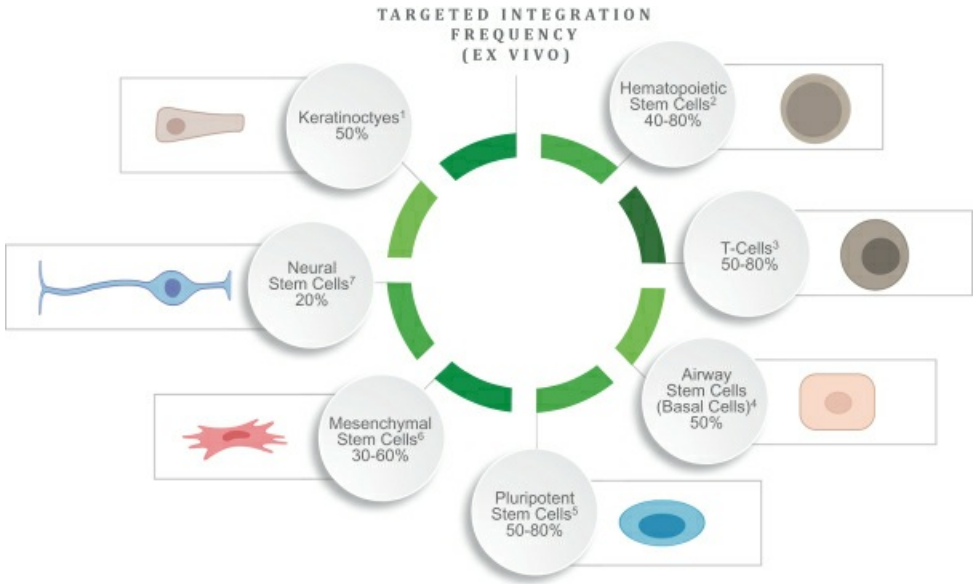


Figure: Targeted gene insertion of the HBA1 gene led to efficient gene insertion and expression in a mouse model

Given high rates of protein production from our gene-targeted cells, we believe that clinically relevant therapeutics can be developed with this approach that require only modest rates of engraftment. We believe that this has the potential to expand the applicability of our targeted gene insertion technology to indications for which risks of random gene integration and chemotherapeutic myeloablative conditioning would be unacceptable.

Other Future Opportunities for Targeted Gene Integration in Other Cell Types and Indications

We intend to pursue applications of our technology platform to develop potential therapies for a number of other genetic diseases including diseases involving the hematopoietic system and other lysosomal storage diseases. We believe that our targeted gene insertion technology, through its ability to lead to the controlled expression of any gene, also has potential to treat diseases outside of monogenic diseases such as the ability to integrate genes to produce next generation CAR effector therapies or myeloid cell therapies for autoimmune disease or oncology. Our high efficiency gene editing technology has been shown using human cells and/or animal models to be applicable to a broad range of HSC-based indications (e.g. MPS1, Krabbe, beta-thalassemia) as well as other tissues, such as airway stem cells (cystic fibrosis), neural stem cells, pluripotent stem cells and keratinocytes (wound healing). We intend to investigate the potential of developing therapies for other diseases based on these findings.



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Manufacturing

We currently have no commercial manufacturing capabilities. For our initial wave of clinical programs, we intend to use qualified third-party contract manufacturing organizations with relevant manufacturing experience in genetic medicines. We have established manufacturing processes for GPH101 and have established relationships with third-party manufacturers with capabilities to manufacture the necessary Drug Substance and Drug Product in accordance with current Good Manufacturing Practices (cGMP). We plan to continue to rely on qualified third-party organizations to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early-stage clinical trials. We expect that commercial quantities of any compound, vector, or engineered cells that we may seek to develop will be manufactured in facilities and by processes that comply with cGMP and relevant health authority regulations. At the appropriate time in the product development process, we will determine whether to establish manufacturing facilities or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop. Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors or contract sales forces to assist in the commercialization of our products. In certain instances, we may consider building our own commercial infrastructure.

As product candidates advance through our pipeline, our commercial plans may change. In particular, some of our research programs target potentially larger indications. Clinical outcomes, the size of the development programs, the size of the target market, and the availability of commercial manufacturing infrastructure will influence our manufacturing strategies in the United States, Europe and the rest of the world.

Competition

The gene therapy and gene 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 currently face, and will continue to face, competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as academic institutions, government agencies and private and public research institutions. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that may become available in the future. Key competitive factors affecting the commercial success of our gene therapies are likely to be efficacy, safety and tolerability profile, reliability, convenience, price and reimbursement.

We compete in the segments of the pharmaceutical, biotechnology, and other related markets that utilize technologies encompassing genomic medicines to create therapies, including gene editing and gene therapy. There are additional companies that are working to develop therapies in areas related to our research programs. Other companies engaged in gene editing and gene therapies include AVROBio, Inc., Beam Therapeutics Inc., bluebird bio, Inc., CRISPR Therapeutics, Inc., Editas Medicine, Inc., Freeline Therapeutics, Homology Medicines, Inc., Intellia Therapeutics, Inc., Mustang Bio, Inc., Orchard Therapeutics plc and Sangamo BioSciences.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product we may commercialize and may render our gene therapies obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our gene therapies. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our gene therapies non-competitive or obsolete.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our platform technology, our programs, and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating any valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing and filing 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. Notwithstanding these efforts, we cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed 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. For more information regarding the risks related to our intellectual property, please see section titled "Risk Factors—Risks Related to Our Intellectual Property."

Our wholly owned and our in-licensed patent applications cover various aspects of our genome editing platform and our programs such as technology platforms directed to genome modification using chemically modified guide RNAs. We intend to continue to pursue, when possible, additional patent protection, including composition of matter, method of use, and process claims, directed to each component of our platform technology and the programs in our portfolio. We also have one option to license patent applications relating to

stable genomic integration in primary cells with CRISPR-Cas and AAV, HSC insertion in alpha globin loci, and HDR correction of IL2RG for treatment of XSCID as well as a second option to license patent applications relating to gene integration in a safe harbor locus CCR5 to correct metabolic diseases, treatment and correction of immunodeficiency conditions, treatment of cystic fibrosis, and treatment of diseases relating via targeting and correcting the alpha globin locus. We also intend to obtain rights to various components of our genome editing platform through one or more licenses from third parties.

As of April 12, 2021, we owned one provisional patent application relating to genome editing and gene replacement for the treatment of beta-thalassemia. If issued as an U.S. patent, and if the appropriate maintenance fees are paid, the U.S. patent would be expected to expire 2042, excluding any additional term for patent term adjustments or patent term extensions.

As of April 1, 2021, we in-licensed one U.S. patent application, and six ex-U.S. patent applications directed to genome modification using chemically modified guide RNA in primary cells from Stanford University. The in-licensed patent applications also relate to use of such genome modifications for therapeutic indications such as SCD. Our current in-licensed patent applications from Stanford, if the appropriate maintenance fees are paid, are expected to expire 2036, excluding any additional term for patent term adjustments or patent term extensions.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment (PTA) which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened (e.g., if a patent is terminally disclaimed over a commonly owned patent having an earlier expiration date). In some instances, such a PTA may result in a U.S. patent term extending beyond 20 years from the earliest date of filing a non-provisional patent application related to the U.S. patent. Patent term extensions (PTE) under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, are also possible for patents that cover an FDA-approved drug as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a PTE of up to five years beyond the expiration of the patent. The length of the PTE is related to the length of time the drug is under regulatory review. PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug, a method for using it, or a method of manufacturing it, may be extended. Similar provisions are available in Europe and certain other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if our products receive regulatory approval, we may be eligible to apply for PTEs on patents covering such products, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such PTE should be granted, and if granted, the length of such PTE. For more information regarding the risks related to our intellectual property, please see section titled "Risk Factors—Risks Related to Our Intellectual Property."

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 seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have implemented measures 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 section titled "Risk Factors—Risks Related to Our Intellectual Property."

Our Material Agreements

Exclusive License Agreement with the Board of Trustees of the Leland Stanford Junior University

In December 2020, we entered into an exclusive license agreement (License Agreement) with The Board of Trustees of the Leland Stanford Junior University (Stanford) pursuant to which Stanford granted us a worldwide license to specified technology and patent rights to develop, manufacture and commercialize human prophylactic and therapeutic products. Other than with respect to specified, broadly applicable assays and procedures and subject to retained rights by Stanford, the license is exclusive with respect to human prophylactic and therapeutic products for the treatment of SCD, XSCID and beta thalassemia. The license is non-exclusive with respect to those broadly applicable assays and procedures and with respect to all human prophylactic and therapeutic products other than for the treatment of SCD, XSCID and beta thalassemia. Please see "Business — Intellectual Property" for additional information concerning the intellectual property related to the License Agreement.

Pursuant to the License Agreement, we paid an upfront license fee of $50,000, and as additional consideration for the license, we agreed to issue to Stanford approximately 1.6 million shares of our common stock. We are obligated to pay Stanford an annual license maintenance fee on each anniversary of the effective date of the License Agreement. The annual license maintenance fee initially is $5,000 and will increase to $50,000 in three increments over the first seven anniversaries of the effective date of the License Agreement. After the first commercial sale of a product falling within the scope of the license (Licensed Product) the annual license maintenance fee is $200,000.

We are required to share with Stanford a portion of any non-royalty income we receive from sublicensing the licensed patent rights or technology, subject to specified exclusions. With respect to sublicenses granted to products for the treatment of SCD, XSCID and beta thalassemia, the portion of sublicense income we must share with Stanford varies by indication and declines from between a mid-teens to a second quartile double-digit percentage prior to the filing of an IND to between a high single-digit to very low double-digit percentage upon achievement of a specified clinical milestone. With respect to sublicenses granted under the licensed technology rights and not licensed patent rights, the portion of sublicense income shared with Stanford declines from between a mid single-digit and very low double-digit percentage prior to the filing of an IND to a low single-digit percentage after filing of an IND.

We are obligated to make payments to Stanford with respect to each Licensed Product of up to an aggregate of $13 million upon the achievement of certain development, regulatory and commercial milestones. Such amounts are payable only once upon the first occurrence of a particular milestone event with respect to each Licensed Product and only once with respect to each new indication covered by any of the Licensed Products.

We also are obligated to pay Stanford low single-digit royalties based on worldwide annual net sales of any Licensed Product, subject to specified reductions. We will be obligated to continue to pay royalties on a Licensed Product-by-Licensed Product and country-by-country basis, until the latest of (a) the expiration of the last valid claim under the licensed patents that covers the sale or manufacture of such Licensed Product in such country, (b) the expiration of any period of regulatory exclusivity with respect to such Licensed Product in such country or (c) the expiration of ten years after the first commercial sale of such Licensed Product in such country.

The term of the License Agreement expires on the later of (a) the expiration of the last patent or abandonment of the last patent application within the license patent rights or (b) the expiration of all royalty terms with respect to Licensed Products. The License Agreement may be terminated by us at will or by Stanford if we remain in breach of the License Agreement following a cure period to remedy the breach.

We are required to use diligent efforts to manufacture, market and sell Licensed Products for the treatment of each of SCD, XSCID and beta thalassemia. In addition, we are required to achieve specified milestones by specified dates with respect to Licensed Products for the treatment of each of SCD, XSCID and beta thalassemia. If we fail to satisfy our diligence obligations, Stanford may terminate the License Agreement for our breach.

Option Agreements with Stanford

First Option Agreement

In January 2021, we entered into an option agreement, or the First Option Agreement, with Stanford, pursuant to which Stanford granted us the right to obtain a license to specified patent rights relating to human prophylactic and therapeutic products. The option may be extended to specified technology at a later date and upon our agreement with Stanford. We may exercise the option in whole or in part to obtain a license under one or more of the optioned patent rights. Subject to retained rights by Stanford, the license is exclusive with respect to human prophylactic and therapeutic products for the treatment of SCD, XSCID and beta thalassemia and non-exclusive with respect to all other human prophylactic and therapeutic products.

Pursuant to the First Option Agreement, we agreed to grant Stanford approximately 300,000 shares of our common stock if we exercise the option and execute and deliver an amendment to the License Agreement that incorporates the optioned patent rights and any optioned technology. Other than such shares of our common stock and a license execution fee of $10,000 if we exercise the option with respect to a particular optioned patent right, no additional payments have been or will be made by us to Stanford under the First Option Agreement or upon the execution of an amendment to the License Agreement that incorporates the optioned patent rights and any optioned technology. The terms of the License Agreement will apply to any Licensed Products falling within the patent rights and technology licensed by us upon exercise of the option.

The term of the First Option Agreement expires 18 months after its effective date, subject to our right to extend such expiration date by up to an additional one year upon notice to Stanford and by another additional one year upon the reasonable agreement of Stanford. The First Option Agreement will terminate if the License Agreement terminates. The First Option Agreement also may be terminated by us at will.

Second Option Agreement

In April 2021, we entered into another option agreement, or the Second Option Agreement, with Stanford, pursuant to which Stanford granted us the exclusive right to obtain a license to specified patent rights relating to human prophylactic and therapeutic products. The option may be extended to specified technology at a later date and upon our agreement with Stanford. We may exercise the option in whole or in part to obtain a license under one or more of the optioned patent rights, subject to a specified waiting period with respect to certain specified patent rights. Subject to retained rights by Stanford and in the case of specified patent rights, the Department of Veterans Affairs, the license will be exclusive with respect to human prophylactic and therapeutic products for the treatment of Gaucher Disease, other diseases treated through insertion of a construct into the CCR5 locus, and diseases treated through insertion of a construct into the alpha globin locus. The license is non-exclusive with respect to all other human prophylactic and therapeutic products.

Pursuant to the Second Option Agreement, we agreed to pay Stanford option fees in an aggregate amount of $30,000 over the term of the option. If we exercise the option with respect to a particular optioned patent right, Stanford and we would negotiate in good faith the terms of a license agreement or an amendment to the License Agreement that incorporates the optioned patent rights and any optioned technology. The terms of the license agreement or amendment could include additional payments to Stanford in excess of those set forth in the License Agreement.

The term of the Second Option Agreement expires 12 months after its effective date, subject to our right to extend such expiration date by two additional one year periods upon notice to and the reasonable agreement of Stanford. The Second Option Agreement may be terminated by us at will or by Stanford if we remain in breach of the Second Option Agreement following a cure period to remedy the breach. The Second Option Agreement also will terminate automatically in the event of a filing of a bankruptcy petition by or against us.

We are required to use diligent efforts to conduct research on potential commercial applications of the optioned patents and any optioned technology. In addition, we are required to use reasonable efforts to achieve

specified milestones during the term of the Second Option Agreement with respect to products incorporating two of therapeutic approaches covered by the optioned patent rights. Our diligence obligations are subject to good faith discussions regarding their modification upon any extension of the term of the Second Option Agreement by us. If we fail to satisfy our diligence obligations Stanford may terminate the Second Option Agreement for our breach.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing.

U.S. Biologics Regulation

In the United States, the FDA regulates biological products under the Federal Food, Drug, and Cosmetic Act (FDCA), and the Public Health Service Act (PHSA), and their implementing regulations. Biological products are also subject to other federal, state, local and foreign statutes and regulations. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may result in delays to the conduct of a study, regulatory review and approval or subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license suspension or revocation, refusal to allow an applicant to proceed with clinical trials, imposition of a clinical hold, issuance of untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations or penalties.

Our product candidates must be approved by the FDA through the Biologics License Application (BLA), process before they may be legally marketed in the United States. The process required by the FDA before biological product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and animal studies performed in accordance with applicable regulations, including the FDA's Good Laboratory Practices (GLPs), regulations and standards;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an independent institutional review board (IRB) or ethics committee representing each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, Good Clinical Practices (GCPs), and other clinical trial-related regulations to establish the safety, purity and potency of the proposed biological product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA, which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labeling;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current Good Manufacturing

Practice requirements (cGMPs) and to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity, and of selected clinical trial sites that generated the data in support of the BLA to assess compliance with the FDA's GCPs;

- satisfactory completion of an FDA Advisory Committee review, if applicable; and
- FDA review and approval, or licensure, of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a product candidate, a sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns, non-compliance, or other issues affecting the integrity of the trial. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial and, once begun, issues may arise that could cause the trial to be suspended or terminated.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight at the local level as set forth in the National Institutes of Health (NIH), Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an Institutional Biosafety Committee (IBC), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding for recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, 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 study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB or ethics committing at or servicing each site at which the clinical trial will be conducted must review and approve the plan for any clinical trial before the clinical trial begins at that site, and must monitor the study until completed. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether 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. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is

unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

There are also requirements governing the reporting of ongoing preclinical studies and clinical trials and clinical study results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

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

- *Phase 1*. The investigational product is typically administered to a small number of healthy volunteers. For gene therapies, the investigational product is typically initially introduced into patients with the target disease or condition. These trials are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with the investigational product, and, if possible, to gain early evidence on effectiveness.
- *Phase 2*. The investigational product is typically administered to a limited patient population to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- *Phase 3*. The investigational product is typically administered to an expanded patient population to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for physician labeling. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA.

When these phases overlap or are combined, the trials may be referred to as Phase 1/2 or Phase 2/3.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and further document clinical benefit in the case of drugs approved under Accelerated Approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the biologic, findings from animal or in vitro testing that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

The FDA, the sponsor or the IRB or may suspend a clinical study at any time on various grounds, including a finding that the research patients 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 candidate has been associated with unexpected serious harm to patients. Additionally, if the trial is being overseen by a data safety monitoring board or committee, this group may recommend halting the clinical trial if it determines that there is an unacceptable safety risk for subjects or on other grounds, such as interim data suggesting a lack of efficacy.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product candidate for one or more indications. The BLA must include all relevant data available from preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product candidate's chemistry, manufacturing, controls, and proposed labeling, among other things. Under the Prescription Drug User Fee Act (PDUFA), as amended, each BLA must be accompanied by a significant application user fee to the FDA, unless a waiver or exemption applies, which is adjusted on an annual basis. The FDA has sixty days from the applicant's submission of a BLA to either issue a refusal to file letter or accept the BLA for filing, indicating that it is sufficiently complete to permit substantive review. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval, and may require additional preclinical, clinical or other studies before it accepts the filing.

Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may be significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product candidate is safe, pure and potent for its intended use, and whether the facility in which it is manufactured, processed, packed or held meets standards designed to assure and preserve the product's identity, safety, strength, quality, and purity. The FDA may convene an advisory committee, typically a panel that includes clinicians and other experts, to provide clinical insight on applications which present difficult questions of safety or efficacy and to 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.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the facility or facilities where the product is manufactured to determine whether the facilities comply with cGMPs. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically audit data from clinical trials to ensure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be manufactured, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the deficiencies that the FDA has identified in the BLA, except that where the FDA

determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification, which may include the potential requirement for additional clinical studies and/or other significant and time-consuming requirements related to preclinical studies and manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even if such data and information is submitted, the FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for a particular indication(s) and may entail limitations on the indicated uses for which such product may be marketed. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. The FDA may also place other conditions on approvals including the requirement of a Risk Evaluation and Mitigation Strategy (REMS), to assure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new product candidates that meet certain criteria. Specifically, product candidates are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. A sponsor may request fast track designation of a product candidate concurrently with, or at any time after, submission of an IND, and the FDA must determine if the product candidate qualifies for such designation within 60 day of receipt of the sponsor's request. The sponsor of a fast track product has opportunities for frequent interactions with the FDA review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant

endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request that a product candidate be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the product candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. The benefits of breakthrough therapy designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers and experienced review staff in a cross-disciplinary review.

As part of the 21st Century Cures Act, Congress amended the FDCA to create an accelerated approval program for RMATs, which include cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a sustained effect on cells or tissues may meet the definition of a RMAT. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. A sponsor may request that FDA designate a product candidate as a regenerative medicine advanced therapy concurrently with or at any time after submission of an IND. 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 new drug application or a BLA for a RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A RMAT that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, 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.

Any marketing application for a product candidate submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for priority review if it has the potential to provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious disease or condition compared to available therapies. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product candidate generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA will require post-marketing restrictions as it deems necessary to assure safe use of the product, such as restricting distribution to certain facilities or physicians with special training or experience or conditioning distribution on the performance of specified medical procedures. The limitations imposed would be commensurate with the specific safety concerns presented by the product. 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.

Fast track designation, breakthrough therapy designation, RMAT designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. 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.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a biological product candidate intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more than individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a product for this type of disease or condition will be recovered from sales in the United States for that product. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic 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 or approval process.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same product 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 or if the holder of the orphan exclusivity cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan exclusivity does not prevent the FDA from approving a different product for the same disease or condition, or the same product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

A designated orphan drug may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Pediatric Trials and Exclusivity

Under the Pediatric Research Equity Act (PREA), a BLA or supplement to a BLA must contain data to assess the safety and efficacy of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDCA requires 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 (PSP), within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. 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 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 nonclinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers. Sponsors who conduct studies of their product candidate in children

are eligible for pediatric exclusivity. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which attaches to the twelve-year exclusivity period for reference biologics, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious of life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects 200,000 or more in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug for such disease or condition will be received from sales in the United States of such drug. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug or biologic application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher (PRV). A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA or BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA or BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program until September 30, 2024, with the potential for PRVs to be granted until September 30, 2026.

Post-Approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims or changes of the site of manufacture, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for each product identified in an approved BLA.

The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. Biological product manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. BLA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

The FDA may withdraw 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 revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning or untitled letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biological products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believethat such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict a manufacturer's communications on the subject of off-label use of their products.

U.S. Patent Term Restoration

Depending upon the timing, duration and specifics of the FDA approval of the use of our biological product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. In addition, a patent can only be extended once and only for a single product. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our patents, if and as applicable, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

Biosimilars and Reference Product Exclusivity

The ACA, includes a subtitle called the Biologics Price Competition and Innovation Act (BPCIA), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic 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 biologic. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

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. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. This does not include a supplement for the biological product or a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength, unless that change is a modification to the structure of the biological product and such modification changes its safety, purity, or potency. 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 that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

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 the European Union, 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 impact the regulatory process in others.

Regulation and Procedures Governing Approval of Medicinal Products in Europe

Clinical Trial Approval

In the European Union, our future products also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the national competent authority (NCA), and one or more independent ethics committees (ECs). Under the current regime all suspected unexpected serious adverse reactions to the investigational drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive. It is expected that the new Regulation will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials foreseen by the Regulation, through an independent audit, currently expected to occur in December 2021. The new Regulation will be directly applicable in all Member States (and so does not require national implementing legislation in each Member State), and aims at simplifying and streamlining the approval of clinical studies in the EU, for instance by providing for a streamlined application procedure via a single point and strictly defined deadlines for the assessment of clinical study applications.

Marketing Authorization

To obtain a marketing authorization for a product in the European Economic Area (EEA) (comprising the EU Member States plus Norway, Iceland and Liechtenstein), an applicant must submit a marketing authorization application, either under the centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EEA Member States (decentralized procedure, national procedure, or mutual recognition procedure).

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EEA. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (i.e. gene therapy, somatic-cell therapy and tissue-engineered products) and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interests of public health.

Specifically, the grant of a marketing authorization in the EEA for products based on genes, tissues or cell, such as gene therapy or somatic-cell therapy medicinal products, is governed in part by Regulation (EC) No 1394/2007 on advanced therapy medicinal products (ATMPs). Regulation (EC) No 1394/2007 lays down specific rules concerning the authorization, supervision, and pharmacovigilance of ATMPs. Manufacturers of ATMPs must demonstrate the quality, safety, and efficacy of their products to the CAT, of the EMA, which provides an opinion on the quality, safety and efficacy of each ATMP subject to marketing authorization application which is sent for final approval to the CHMP, of the EMA. The CHMP recommendation is then sent to the European Commission, which adopts a decision on whether to grant a marketing authorization which is binding in all Member States. Under the centralized procedure, the maximum timeframe for the evaluation of a marketing authorization application is 210 days from receipt of a valid application, excluding clock stops when additional

information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of a marketing authorization application considerably beyond 210 days. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA), the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

European Data and Marketing Exclusivity

In the EEA, innovative medicinal products (including both small molecules and biological medicinal products), qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies. Even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on an application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

European Orphan Designation and Exclusivity

In the EEA, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions which either affect no more than 5 in 10,000 persons in the EU, or where it is unlikely that the marketing of the medicine would generate sufficient return to justify the necessary investment in its development. In each case, no satisfactory method of diagnosis, prevention or treatment of the condition must have been authorized (or, if such a method exists, the product in question would be of significant benefit to those affected by the condition).

In the EEA, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers, and ten years of market exclusivity is granted following marketing approval for the orphan product. This period may be reduced to six years if, at the end of the fifth year, it is established that the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. During the period of market exclusivity, marketing authorization may

only be granted to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the UK voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty and the UK formally left the EU on January 31, 2020. A transition period began on February 1, 2020, during which EU medicines legislation remained applicable to the UK, which ended on December 31, 2020. Since the regulatory framework in the UK covering the quality, safety and efficacy of medicinal products, clinical trials, marketing authorization, commercial sales and distribution of medicinal products is derived from EU Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the UK, as UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA, the UK medicines and medical devices regulator, has published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products. In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We or our collaborators may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical 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 obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, 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.

The marketability of any product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care 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 or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other U.S. Healthcare Laws and Compliance Requirements

Healthcare providers, including physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we may develop for which we obtain marketing approval. Our current and future arrangements with third-party payors, healthcare providers and customers may implicate broadly applicable fraud and abuse and other healthcare laws and regulations. Restrictions under applicable federal and state healthcare laws and regulations, including certain laws and regulations applicable only if we have marketed products, include the following:

- the civil False Claims Act (FCA), prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the 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 False Claims Act can result in very significant monetary penalties, for each false claim and treble the amount of the government's damages. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;
- the federal Anti-Kickback Statute prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. 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. A violation of the federal Anti-Kickback Statute can also form the basis for FCA liability;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the 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 (HITECH), and its implementing regulations, including the final omnibus rule published on January 25, 2013, imposes, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes

HIPAA's privacy and security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain, transmit, or obtain, protected health information in connection with providing a service for or on behalf of a covered entity, and their covered subcontractors. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions;

- the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;
- federal transparency laws, including the federal Physician Payment Sunshine Act created under the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), and its implementing regulations, which requires manufacturers of certain drugs, devices, medical supplies, and biologics, among others, to track and disclose payments under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) and other transfers of value they make to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. This information is subsequently made publicly available in a searchable format on a Centers for Medicare & Medicaid Services (CMS), website. Failure to disclose required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and/or other healthcare providers; and
- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

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. The provision of benefits or advantages to also induce or reward improper performance generally is governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the United Kingdom. Infringement of these laws could result in substantial fines and imprisonment. EU

Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the EU.

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

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies.

Within the United States, the federal government and individual states have aggressively pursued healthcare reform, as evidenced by the passing of the ACA and the ongoing efforts to modify or repeal that legislation. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Modifications have been implemented under the previous presidential administration and additional modifications or repeal may occur.

There have been executive, judicial and congressional challenges to certain aspects of the ACA. For example, the U.S. Supreme Court is currently reviewing the constitutionality of the ACA, but it is unknown when a decision will be reached On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. Although the Supreme Court has not yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage

through Medicaid or the ACA. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction, asked 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 up to 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester reductions from May 1, 2020 through December 31, 2021. On January 2, 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, 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. The Bipartisan Budget Act (BBA), also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Furthermore, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS, issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. At the state level, legislatures have also been increasingly passing legislation and implementing

regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Employees and Human Capital Resources

As of March 31, 2021, we had 27 full-time employees, including eight with Ph.D. or M.D. degrees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Facilities

We lease a 6,340 square foot office space, located at 279 East Grand Avenue, Suite 430, South San Francisco, CA 94080 and intend to move into a 19,195 square foot laboratory facility, located at 201 Haskins Way, South San Francisco, CA 94080 upon completion of certain modifications. The office lease expires upon delivery of the laboratory space and in no event sooner than September 2021. The laboratory facility lease expires 42 months from the date it is delivered to us. We believe that our current facilities are sufficient to meet our current and near-term needs. We believe that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Legal Proceedings

We are not currently a party to any material legal proceedings. From time to time, we may, however, in the ordinary course of business face various claims brought by third parties, and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation, and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

As of the date of this prospectus, we were not party to any legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors, including their ages, as of April 15, 2021.

Name	Age	Position(s)
Executive Officers and Employee Directors:		
Josh Lehrer, M.D.	47	Chief Executive Officer and Director
Katherine V. Stultz	47	Chief Operating Officer
Philip P. Gutry	47	Chief Business Officer, Head of Finance & Investor Relations
Jerry Cacia	54	Chief Technical Officer
Non-Employee Directors:		
Perry Karsen	66	Director and Board Chair
Abraham Bassan	36	Director
Jerel Davis, Ph.D.	44	Director
Kristen M. Hege, M.D.	57	Director
Joseph Jimenez	61	Director
Matthew Porteus, M.D., Ph.D.	56	Director
Carlo Rizzuto, Ph.D.	50	Director
Smital Shah	44	Director
Jo Viney, Ph.D.	55	Director

Executive Officers and Employee Directors

Josh Lehrer, M.Phil., M.D., FACC currently serves as our chief executive officer and on our board of directors since April 2020. From October 2013 to April 2020, Dr. Lehrer held various leadership roles at Global Blood Therapeutics, Inc., including chief medical officer. From September 2009 to October 2013, Dr. Lehrer served in leadership roles at Genentech in clinical development and business development. Dr. Lehrer has also held attending physician roles at Stanford University Medical Center and the Palo Alto Veteran's Affairs Health System. He holds an A.B. in Biochemical Sciences from Harvard University and a Master of Philosophy in Biological Sciences from the University of Cambridge. Dr. Lehrer earned his Doctor of Medicine at the University of California, San Francisco (UCSF), School of Medicine and completed his residency at UCSF in internal medicine. Dr. Lehrer served as a clinical and postdoctoral fellow in cardiovascular medicine at Stanford University and attended the Institute for Entrepreneurship at the Stanford Graduate School of Business. We believe that Dr. Lehrer is qualified to serve on our board of directors based on his medical background, extensive experience in business and clinical development and knowledge of private and public development stage biotechnology companies.

Katherine Vega Stultz has served as our chief operating officer since August 2020. Prior to joining Graphite Bio, Ms. Stultz spent 15 years at Celgene Corporation. She served most recently as general manager in the Spain/Portugal market. Earlier at Celgene, Ms. Stultz served as corporate vice president, global project leadership, hematology and oncology, directing the clinical project organization worldwide and overseeing over 30 mid/late stage clinical programs. Ms. Stultz began her career at Eli Lilly & Company and ConvaTec, a Bristol-Myers Squibb company, where she progressed through a series of product development, project management, sales, and marketing positions. Ms. Stultz holds a B.S. in Mechanical Engineering (Biomedical Applications) from Cornell University and has attended executive leadership development programs at the Darden School of Business, University of Virginia, IESE Business School in Barcelona, Spain, and the International Institute for Management Development (IMD) in Switzerland.

Philip P. Gutry serves as our chief business officer, head of finance & investor relations, a role he has held since October 2020. Mr. Gutry brings to this role extensive business development, strategy, finance and investor relations experience with a successful track record of raising capital and establishing partnerships for biotech companies. Prior to joining Graphite Bio, Mr. Gutry worked at Kronos Bio, Inc. a clinical-stage oncology company focused on targeting dysregulated transcription, where he served as chief business officer from October 2018 to October 2020. Previously, Mr. Gutry served as the executive director of business development at Regeneron Pharmaceuticals, Inc. from June 2015 to October 2018, a principal at MPM Capital from June 2011 to June 2015 and the associate director of corporate development at Gilead Sciences, Inc. from August 2006 to May 2011. Mr. Gutry also serves on the board of directors at Cerecor Inc., a biopharmaceutical company focused on the development and commercialization of products in rare pediatric and orphan diseases. Mr. Gutry received his A.B. in Earth Sciences from Dartmouth College and his M.B.A. in Healthcare Management from The Wharton School of the University of Pennsylvania.

Jerry Cacia has served as our chief technical officer since April 2021. From January 2016 to February 2021, Mr. Cacia was employed at F. Hoffmann-La Roche AG, where he first served as the head of biologics and drug product manufacturing, and subsequently as the head of global technical development. Mr. Cacia began his career at Genentech in October 1988 and held various senior leadership roles until he left the company in January 2016, including head of global manufacturing science and technology and head of biologics process development. Mr. Cacia received his B.A. in Biological Sciences from the University of California, Santa Cruz.

Non-Employee Directors

Perry Karsen has served as the chair of our board of directors since October 2020 and as a member of our board of directors since June 2020. Mr. Karsen is currently a venture partner at Samsara BioCapital, L.P. and the executive chair of Autobahn Labs, Inc. From May 2013 to December 2015, Mr. Karsen was the chief executive officer of Celgene Cellular Therapeutics, Inc., a division of Celgene Corporation. Mr. Karsen served as chief operations officer and executive vice president of Celgene from July 2010 to May 2013, and as senior vice president and head of worldwide business development of Celgene from 2004 to 2009. Between February 2009 and July 2010, Mr. Karsen was chief executive officer of Pearl Therapeutics Inc., subsequently acquired by AstraZeneca plc. Prior to his tenure with Celgene, Mr. Karsen held executive positions at Human Genome Sciences, Inc., a publicly traded biotechnology company, since acquired by GlaxoSmithKline plc; Bristol-Myers Squibb Co.; Genentech, Inc., since acquired by Hoffmann-La Roche AG (Roche); and Abbott Laboratories. In addition, Mr. Karsen served as a general partner at Pequot Ventures. He has been a member of the boards of directors of several publicly traded biotechnology companies, including Voyager Therapeutics, Inc. since July 2015, Intellia Therapeutics, Inc. since April 2016, Jounce Therapeutics, Inc. since January 2016, and OncoMed Pharmaceuticals, Inc. since January 2016. Mr. Karsen has served as chairman of the boards of directors of Intellia and Jounce since April 2016 and executive chairman of the board of OncoMed since 2018. Mr. Karsen was formerly a member of the boards of directors of the public biotechnology companies Alliqua Biomedical, Inc. from December 2013 to February 2016 and Agios Pharmaceuticals, Inc. from November 2011 to March 2016. Mr. Karsen was also formerly a member of the boards of directors of the Biotechnology Innovation Organization (BIO) and the Alliance for Regenerative Medicine. Mr. Karsen received his B.S. in Biological Sciences from the University of Illinois, Urbana-Champaign, a Masters of Management from Northwestern University's Kellogg Graduate School of Management and an M.A.T. of Biology from Duke University. We believe that Mr. Karsen's executive leadership experience, including his experience as an executive at large and successful multi-national pharmaceutical companies and membership on board of directors of various publicly traded biotechnology companies, qualifies him to serve as a member of the board of directors.

Abraham Bassan has served on our board of directors since June 2020. Since July 2017, Mr. Bassan has served as a vice president at Samsara BioCapital. Before joining Samsara BioCapital, Mr. Bassan was the director of program biology at Revolution Medicines, Inc. from October 2015 to July 2017 and its director of project management from December 2014 to September 2015. Mr. Bassan was the founder and chief executive officer of Aurora Medical, Inc. from September 2012 to September 2014. Mr. Bassan was also the associate

director of program development at bluebird bio, Inc. from May 2010 to August 2012. Mr. Bassan received his A.B. in Molecular Biology from Princeton University and a M.S. in Development Biology from Stanford University. We believe that Mr. Bassan is qualified to serve on our board of directors based on his significant knowledge of the life sciences industry and experience and expertise in evaluating and investing in life sciences companies.

Jerel Davis, Ph.D. has served on our board of directors since our inception in October 2019. Since June 2011, Dr. Davis has served at Versant Venture Management, LLC, a healthcare investment firm, where he has held the position of managing director since 2015. He has served on the boards of directors of many public and private biotech companies including BlueRock Therapeutics LP, Turnstone Biologics Inc., Chinook Therapeutics, Inc., Inception 5 Inc. and Northern Biologics Inc. Prior to joining Versant, Dr. Davis was an associate principal at McKinsey & Company in various healthcare markets including the United States, Canada, Europe and China. He received a B.S. in Mathematics and Biology from Pepperdine University and a Ph.D. in Population Genetics from Stanford University. We believe that Dr. Davis's broad and extensive experience in the life sciences industry as both an investor of and launching numerous life sciences companies qualifies him to serve on our board of directors.

Kristen M. Hege, M.D. has served on our board of directors since April 2021. Dr. Hege joined Celgene Corporation in 2010 as vice president of translational development and is currently the senior vice president of early clinical development of hematology/oncology and cell therapy at Bristol Myers Squibb Company (following its acquisition of Celgene in 2019). Dr. Hege has also held an active faculty position at the University of California, San Francisco Medical Center since 1996, most recently as the clinical professor of medicine of hematology/oncology, serving in that role as a volunteer since 2008. Prior to Celgene, Dr. Hege served as the chief medical officer at Cellerant Therapeutics and acting chief medical officer at Aragon Pharmaceuticals and Theraclone Sciences. Dr. Hege was also the vice president of clinical research and development at Cell Genesys. Dr. Hege previously served as a volunteer-at-large director for the Society for Immunotherapy of Cancer from 2016 to 2019 and the BayBio/California Life Sciences Association from 2014 to 2016. Dr. Hege has served on the board of directors of Mersana Therapeutics, Inc. since August 2016. She also previously served as a member of the board of directors at Arcus Biosciences from 2018 to 2019 and as a board observer for Flexus Biosciences from 2014 to 2015. Dr. Hege received a B.A. in Biochemistry from Dartmouth College summa cum laude, an M.D. from University of California, San Francisco and Board certification in hematology and medical oncology from the University of California, San Francisco. We believe that Dr. Hege's medical background and experience in the biotechnology industry qualify her to serve as a director.

Joseph Jimenez has served on our board of directors since June 2020. Mr. Jimenez is theco-founder and managing partner of Aditum Bio, a biotechnology venture fund, where he has served since August 2019. He is the former chief executive officer of Novartis AG, a position he held from 2010 to 2018. Prior to this role, Mr. Jimenez held several senior positions at Novartis from 2007 to 2010, including division head of Novartis Pharmaceuticals and leadership of the company's Consumer Health Division. Mr. Jimenez also held various leadership roles at H. J. Heinz Company in Europe and North America from 1999 to 2006 and at ConAgra Foods from 1993 to 1998 and was an advisor to the Blackstone Group L.P. from 2006 to 2007. Mr. Jimenez has been a member of the board of directors of General Motors since 2015, Procter & Gamble since 2018 and Century Therapeutics since 2019. Mr. Jimenez received a B.A. in Economics from Stanford University and an M.B.A. from University of California, Berkeley's Haas School of Business. We believe that Mr. Jimenez is qualified to serve on our board of directors based on his extensive leadership experience and executive leadership at various technology companies.

Matthew Porteus, M.D., Ph.D. has served on our board of directors since March 2020. Dr. Porteus is an associate professor of pediatrics of the Department of Pediatrics, Divisions of Hematology/Oncology and Human Gene Therapy, at Stanford School of Medicine, where he has served in various leadership roles since October 2010. Prior to joining Stanford, Dr. Porteus served as an assistant professor at the University of Texas Southwestern Medical Center from 2003 to 2010. His research focuses on developing homologous

recombination-based therapies for genetic and other diseases. Dr. Porteus also maintains a clinical practice at the Lucille Packard Children's Hospital, where he is an attending physician for the Pediatric Bone Marrow Transplant Service. Dr. Porteus graduated Magna Cum Laude with an A.B. in History and Science from Harvard University and completed his M.D. and Ph.D. degrees at Stanford University. Dr. Porteus completed his residency training in pediatrics at Boston Children's Hospital, and fellowship training in Pediatric Hematology/Oncology at Boston Children's Hospital and the Dana Farber Cancer Institute. For his post-doctoral work, Dr. Porteus trained at the Massachusetts Institute of Technology and the California Institute of Technology. During this time, he began studying gene editing and was the first to show that engineered nucleases could be used to precisely modify human cells by homologous recombination. We believe that Dr. Porteus is qualified to serve on our board of directors based on his medical background and extensive knowledge surrounding genetic diseases, gene therapy and gene editing.

Carlo Rizzuto, Ph.D. has served on our board of directors since March 2020. Dr. Rizzuto joined Versant Ventures in November 2012 as an operating principal, became a venture partner in 2015 and a partner in 2017. He was previously employed at Novartis Pharmaceuticals, where he was the global program team director, from July 2010 to October 2012. Dr. Rizzuto has served on the board of directors of Pandion Therapeutics, Inc. since January 2018. Dr. Rizzuto received a B.A. in biology from the University of Virginia and a Ph.D. in virology from Harvard University. We believe that Dr. Rizzuto's experience as an investor in the life sciences industry qualifies him to serve on our board of directors.

Smital Shah, M.B.A. has served as a member of our board of directors since April 2021. Since October 2014, Ms. Shah has served in roles of increasing responsibility at ProQR Therapeutics NV, a rare disease company, including as chief financial officer from October 2014 to December 2018 and most recently as chief business and financial officer since December 2018. Previously, Ms. Shah served as a corporate treasurer at Gilead Sciences, Inc. from August 2012 to September 2014. Prior to Gilead, she was an investment banker at Leerink Partners and JP Morgan focused on capital raising and strategic transactions in the biotechnology space. Previously, Ms. Shah held various research and development roles at Johnson & Johnson Company. Since March 2019, Ms. Shah has served on the board of directors of Pliant Therapeutics, Inc. Ms. Shah holds a B.S. in Chemical Engineering from the University of Mumbai, a M.S. in Chemical Engineering from Virginia Tech and an M.B.A. from the University of California, Berkeley Haas School of Business. We believe that Ms. Shah is qualified to serve on our board of directors due to her extensive experience in the life sciences industry and her leadership experience as a senior financial executive.

Jo Viney, Ph.D. has served as a member of our board of directors since March 2021. Dr. Viney is a co-founder and has served as chief scientific officer of Pandion Therapeutics, Inc. since April 2017, and as its president since July 2019. Pandion Therapeutics was acquired by Merck & Co in April 2021. Jo continues to serve as president and chief scientific officer of Pandion Therapeutics, now as a wholly-owned subsidiary of Merck & Co (known as MSD outside Canada and the US). From November 2015 to November 2016, Dr. Viney served as senior vice president of drug discovery at Biogen Inc., after serving as vice president of immunology research from July 2011 to October 2015. From September 2003 to April 2011, Dr. Viney served as executive director of inflammation research at Amgen, Inc., after serving as director of inflammation research from July 2002 to August 2003. Dr. Viney has served on the board of directors of Harpoon Therapeutics, Inc. since July 2020 and on the board of directors of Finch Therapeutics Group, Inc. since August 2019, and has previously served and currently serves on the boards of directors of several private companies. Dr. Viney has a B.Sc. from the University of East London and a Ph.D. in immunology from the University of London, St. Bartholomew's Hospital Medical School. We believe that Dr. Viney's substantial leadership experience in the biotechnology industry qualifies her to serve on our board of directors.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Composition of Our Board of Directors

Our board of directors consists of ten members, each of whom are members pursuant to the board composition provisions of our certificate of incorporation and agreements with our stockholders. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and corporate governance committee and our board of directors may consider a broad range of factors relating to the qualifications and background of nominees. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is to identify persons who will further the interests of our stockholders through his or her established record of professional accomplishments, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence

Upon the completion of this offering, we expect that our common stock will be listed on the Nasdaq Global Market. Applicable rules of Nasdaq require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, (1) on the date of the completion of the offering, at least one member of each of a listed company's audit, compensation and nominating and corporate governance committees be independent, (2) within 90 days of the date of the completion of the offering, a majority of the members of such committees be independent and (3) within one year of the date of the completion of the offering, all the members of such committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

Our board of directors has determined that all members of the board of directors, except Drs. Lehrer and Porteus, are independent directors, including for purposes of the rules of Nasdaq and the SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock and with licensors and service providers of our Company. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC, subject to the transition rules described above for newly listed companies. Dr. Lehrer is not an independent director under these rules because he is currently employed as the chief executive officer of our Company and Dr. Porteus is not an independent director under these rules because he is currently providing services as a paid consultant of our Company and has an affiliation with a licensor and service provider of our Company.

Staggered Board

In accordance with the terms of our amended and restated certificate of incorporation that will become effective immediately prior to the closing of this offering and our amended and restated by-laws that will become effective on the date on which the registration statement of which this prospectus is part is declared effective by the SEC, our board of directors will be divided into three staggered classes of directors and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2022 for Class I directors, 2023 for Class II directors and 2024 for Class III directors.

- Our Class I directors will be ; ; and .
- Our Class II directors will be ; ; and .
- Our Class III directors will be ; ; and .

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective immediately prior to the closing of this offering will provide that the number of directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Board Leadership Structure and Board's Role in Risk Oversight

Perry Karsen is our current chair of the board and Josh Lehrer, M.D. is our current chief executive officer, hence the roles of chair and the chief executive officer and president are separated. We plan to keep these roles separated following the completion of this offering. We believe that separating these positions allows our president and chief executive officer to focus on setting the overall strategic direction of the company, expanding the organization to deliver on our strategy and overseeing our day-to-day business, while allowing the chair of the board to lead the board of directors in its fundamental role of providing strategic advice. Our board of directors recognizes the time, effort and energy that the president and chief executive officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our chair of the board, particularly as the board of directors' oversight responsibilities continue to grow. While our amended and restated bylaws and corporate governance guidelines do not require that our chair of the board and president positions be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations, strategic direction and intellectual property as more fully discussed in the section titled "Risk Factors" appearing elsewhere in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees below and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for

evaluating and overseeing the management of a particular risk or risks, the chairperson of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

Committees of Our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will operate pursuant to a charter adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus is a part. Upon the effectiveness of the registration statement of which this prospectus is a part, the composition and functioning of all of our committees will comply with all applicable requirements of SOX, Nasdaq and SEC rules and regulations.

Audit Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, , and will serve on the audit committee, which will be chaired by . Our board of directors has determined that are "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable Nasdaq rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated as an "audit committee financial expert," as defined under the applicable rules of the SEC. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independentregistered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

Compensation Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, , and will serve on the compensation committee, which will be chaired by . Our board of directors has determined that each member of the compensation committee is "independent" as defined in the applicable Nasdaq rules. The compensation committee's responsibilities include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our principal executive officer;
- evaluating the performance of our principal executive officer in light of such corporate goals and objectives and based on such evaluation: (i) determining cash compensation of our principal executive officer; and (ii) reviewing and approving grants and awards to our principal executive officer under equity-based plans;
- reviewing and approving or recommending to the board of directors the cash compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing the compensation committee report required by SEC rules, if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention, termination or compensation of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Nominating and Corporate Governance Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, , and will serve on the nominating and corporate governance committee, which will be chaired by . Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as defined in the applicable Nasdaq rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

We intend to adopt a written code of business conduct and ethics, effective upon the effectiveness of the registration statement of which this prospectus is a part, that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following the effectiveness of the registration statement of which this prospectus is a part, a current copy of the code will be posted on the investor relations section of our website, which is located at https://graphitebio.com/. The inclusion of our website address in this prospectus does not incorporate by reference the information on or accessible through our website into this prospectus. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, will contain provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Each of our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective immediately prior to the completion of this offering, will provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws will also obligate us to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage.

EXECUTIVE COMPENSATION

Overview

The following discussion contains forward-looking statements that are based on our current plans and expectations regarding our future compensation programs. The actual amount and form of compensation that we pay and the compensation policies and practices that we adopt in the future may differ materially from the currently-planned programs that are summarized in this discussion

The compensation provided to our named executive officers for the fiscal year ended December 31, 2020 is detailed in the 2020 Summary Compensation Table and accompanying footnotes and narrative that follow. Our named executive officers for the fiscal year ended December 31, 2020, which consists of our Chief Executive Officer and our two most highly-compensated individuals (other than our Chief Executive Officer) who were serving as executive officers on December 31, 2020, are:

- Josh Lehrer, M.D., our Chief Executive Officer;
- Katherine V. Stultz, our Chief Operating Officer; and
- Philip P. Gutry, our Chief Business Officer, Head of Finance & Investor Relations.

2020 Summary Compensation Table

The following table provides information regarding the total compensation awarded to, earned by, and paid to our named executive officers for services rendered to us in all capacities for the fiscal year ended December 31, 2020.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Stock Awards ($)(2)	Option Awards ($)(3)	Non-equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Josh Lehrer, M.D., Chief Executive Officer(4)	2020	298,045	133,880	23,138	—	—	—	455,063
Katherine V. Stultz, Chief Operating Officer(5)	2020	133,333	202,500	—	414,814	—	—	750,647
Philip P. Gutry, Chief Business Officer, Head of Finance & Investor Relations(6)	2020	90,909	79,540	—	536,216	—	—	706,665

(1) Represents discretionary bonuses earned by our named executive officers, based on our achievement of certain corporate performance goals for 2020, as well as a $150,000 signing bonus for Ms. Stultz and a $50,000 signing bonus for Mr. Gutry, in each case received in connection with their commencement of employment with us in 2020.

(2) The amounts reported represent the aggregate grant date fair value of the restricted stock awards granted to our named executive officers during the 2020 fiscal year, calculated in accordance with Financial Accounting Standards Board (FASB), Accounting Standards Codification (ASC), Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the restricted stock awards reported in this column are set forth in notes 2 and 11 of our financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these restricted stock awards and do not correspond to the actual economic value that may be received by our named executive officers upon the vesting of the restricted stock awards or any sale of the underlying shares of common stock.

(3) The amounts reported represent the aggregate grant date fair value of the stock options granted to our named executive officers during the 2020 fiscal year, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in notes 2 and 11 of our financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these stock options and do not correspond to the actual economic value that may be received by our named executive officers upon the exercise of the stock options or any sale of the underlying shares of common stock.

(4) Dr. Lehrer commenced employment with us on April 20, 2020 and his 2020 base salary and 2020 bonus were pro-rated accordingly.

(5) Ms. Stultz commenced employment with us on August 31, 2020 and her 2020 base salary and 2020 bonus were pro-rated accordingly.

(6) Mr. Gutry commenced employment with us on October 5, 2020 and his 2020 base salary and 2020 bonus were pro-rated accordingly.

Narrative to Summary Compensation Table

Base Salaries

The annual base salaries for Dr. Lehrer, Ms. Stultz and Mr. Gutry for the year ended December 31, 2020 were $425,000, $400,000 and $375,000, respectively. Dr. Lehrer, Ms. Stultz and Mr. Gutry commenced employment with the Company on April 20, 2020, August 31, 2020 and October 5, 2020, respectively, and their annual base salaries were pro-rated accordingly for the 2020 fiscal year.

Bonuses

Annual Bonuses

During the fiscal year ended December 31, 2020, our named executive officers were eligible to earn a discretionary annual bonus based on the achievement of certain Company performance objectives. For the fiscal year ended December 31, 2020, the target annual bonuses for Dr. Lehrer, Ms. Stultz and Mr. Gutry were 40%, 30% and 30%, respectively, of the applicable named executive officer's annual base salary, prorated as applicable based on their commencement date. For the fiscal year ended December 31, 2020, the Company achieved 105% of its Company performance objectives.

Signing Bonuses

In connection with their commencement of employment with us, Ms. Stultz and Mr. Gutry received signing bonuses of $150,000 and $50,000, respectively.

Equity Compensation

During the fiscal year ended December 31, 2020, we granted restricted stock awards to our Chief Executive Officer and a stock option award to each of our other named executive officers, as described in more detail in the "Outstanding Equity Awards at Fiscal 2020 Year-End" table.

Perquisites or Personal Benefits

We do not provide significant perquisites or personal benefits to our employees with an aggregate equal to or greater than $10,000.

401(k) Plan

We maintain a tax-qualified retirement plan (the 401(k) Plan) that provides eligible U.S. employees with an opportunity to save for retirement on a tax-advantaged basis. Plan participants are able to defer eligible compensation subject to applicable annual Internal Revenue Code limits. We may provide matching contributions under the 401(k) Plan, but did not provide any such contributions during the 2020 fiscal year. The 401(k) Plan is intended to be qualified under Section 401(a) of the Internal Revenue Code with the 401(k) Plan's related trust intended to be tax exempt under Section 501(a) of the Internal Revenue Code. As a tax-qualified retirement plan, contributions to the 401(k) Plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) Plan.

Executive Employment Arrangements

We have entered into an offer letter with each of the named executive officers in connection with his or her employment with us, which set forth the terms and conditions of his or her employment. Each named executive officer has also entered into our standard proprietary information and inventions agreement.

Offer Letters in Place During the Fiscal Year Ended December 31, 2020 for Our Named Executive Officers

Josh Lehrer, M.D.

On February 28, 2020, we entered into an offer letter with Dr. Lehrer, (the Lehrer Letter) for the position of Chief Executive Officer. The Lehrer Letter provides for Dr. Lehrer's at-will employment. Mr. Lehrer's current annual base salary is $425,000, which is subject to periodic review and adjustment. Dr. Lehrer is eligible to earn an annual bonus with a target amount equal to 40% of his annual base salary and to participate in the employee benefit plans generally available to our employees. The Lehrer Letter also provides for Dr. Lehrer's initial grant of restricted stock, which vests 25% on the 12-month anniversary of his start date and in monthly installments thereafter for the next three years, subject to in case to Dr. Lehrer's continuous service with the Company through each applicable date.

Pursuant to the Lehrer Letter, in the event that Dr. Lehrer's employment is terminated by us without "cause" or Dr. Lehrer resigns for "good reason" (as each term is defined in the Lehrer Letter) (each, a Qualifying Event), subject to the execution and effectiveness of a general release of claims, he will be entitled to receive (i) if the Qualifying Event occurs prior to the first date on which we have sold preferred stock with aggregate gross proceeds of at least $20,000,000 cumulatively to such date (Second Tranche Closing), (A) then six months' base salary continuation and (B) subject to Dr. Lehrer's timely election to continue COBRA health coverage, six (6) months of the employer-paid portion of his COBRA premiums or (ii) if the Qualifying Event occurs after the Second Tranche Closing, (A) then twelve (12) months' base salary continuation and (B) subject to Dr. Lehrer's timely election to continue COBRA health coverage, twelve (12) months of the employer-paid portion of his COBRA premiums. Additionally, if a Qualifying Event other than death or disability occurs within three (3) months prior to and twelve (12) months after a "change in control" (as defined the Lehrer Letter), Dr. Lehrer will be entitled to 100% acceleration of vesting of his equity award grants.

The payments and benefits provided under the Lehrer Letter in connection with a change in control may not be eligible for a federal income tax deduction by us pursuant to Section 280G of the Internal Revenue Code. These payments and benefits may also subject Dr. Lehrer to an excise tax under Section 4999 of the Internal Revenue Code. If the payments or benefits payable to an eligible participant in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Internal Revenue Code, then those payments or benefits will be reduced if such reduction would result in a greater net after-tax benefit to Dr. Lehrer.

Katherine V. Stultz

On August 3, 2020, we entered into an offer letter with Ms. Stultz, (the Stultz Letter) for the position of Chief Operating Officer. The Stultz Letter provides for Ms. Stultz's at-will employment. Ms. Stultz's current annual base salary is $400,000, which is subject to periodic review and adjustment. Ms. Stultz is eligible to earn an annual bonus with a target amount equal to 30% of her annual base salary and to participate in the employee benefit plans generally available to our employees. In addition, the Stultz Letter provides for a one-time signing bonus equal to $150,000, subject to repayment if Ms. Stultz voluntarily terminates her employment (other than for "good reason," as defined in the Stultz Letter) prior to the twelve (12) month anniversary of her start date. The Stultz Letter also provides for Ms. Stultz's initial stock option grant, which vests 25% on the 12-month anniversary of her start date and in monthly installments thereafter for the next three years, subject to in case to Ms. Stultz's continuous service with the Company through each applicable date.

Pursuant to the Stultz Letter, in the event that Ms. Stultz's employment is terminated by us without "cause" or Ms. Stultz resigns for "good reason" (as each term is defined in the Stultz Letter) (each, a Qualifying Event), subject to the execution and effectiveness of a general release of claims, she will be entitled to receive, if the Qualifying Event occurs after the Second Tranche Closing, (i) three (3) months' base salary continuation and (ii) subject to the Ms. Stultz's timely election to continue COBRA health coverage, three (3) months of the

employer-paid portion of her COBRA premiums. Additionally, if a Qualifying Event other than death or disability occurs within three (3) months prior to and twelve (12) months after a "change in control" (as defined the Stultz Letter), Ms. Stultz will be entitled to 100% acceleration of vesting of all her equity award grants.

The payments and benefits provided under the Stultz Letter in connection with a change in control may not be eligible for a federal income tax deduction by us pursuant to Section 280G of the Internal Revenue Code. These payments and benefits may also subject Ms. Stultz to an excise tax under Section 4999 of the Internal Revenue Code. If the payments or benefits payable to an eligible participant in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Internal Revenue Code, then those payments or benefits will be reduced if such reduction would result in a greater net after-tax benefit to Ms. Stultz.

Philip P. Gutry

On September 14, 2020, we entered into an offer letter with Mr. Gutry, (the Gutry Letter) for the position of Chief Business Officer and Head of Finance and Investor Relations. The Gutry Letter provides for Mr. Gutry's at-will employment. Mr. Gutry's current annual base salary is $375,000, which is subject to periodic review and adjustment. Mr. Gutry is eligible to earn for an annual bonus with a target amount equal to 30% of his annual base salary and to participate in the employee benefit plans generally available to our employees. In addition, the Gutry Letter provides for a one-time signing bonus equal to $50,000, subject to repayment if Mr. Gutry voluntarily terminates his employment prior to the twelve (12) month anniversary of his start date. The Gutry Letter also provides for Mr. Gutry's initial stock option grant, which vests 25% on the 12-month anniversary of his start date and in monthly installments thereafter for the next three years, subject to in case to Mr. Gutry's continuous service with the Company through each applicable date.

Pursuant to the Gutry Letter, in the event that Mr. Gutry's employment is terminated by us without "cause" or Mr. Gutry resigns for "good reason" (as each term is defined in the Gutry Letter) (each, a Qualifying Event), subject to the execution and effectiveness of a general release of claims, he will be entitled to receive, if the Qualifying Event occurs after the Second Tranche Closing, (i) three (3) months' base salary continuation and (ii) subject to the Mr. Gutry's timely election to continue COBRA health coverage, three (3) months of the employer-paid portion of his COBRA premiums. Additionally, if a Qualifying Event other than death or disability occurs within three (3) months prior to and twelve (12) months after a "change in control" (as defined the Gutry Letter), Mr. Gutry will be entitled to 100% acceleration of vesting of all his equity award grants.

The payments and benefits provided under the Gutry Letter in connection with a change in control may not be eligible for a federal income tax deduction by us pursuant to Section 280G of the Internal Revenue Code. These payments and benefits may also subject Mr. Gutry to an excise tax under Section 4999 of the Internal Revenue Code. If the payments or benefits payable to an eligible participant in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Internal Revenue Code, then those payments or benefits will be reduced if such reduction would result in a greater net after-tax benefit to Mr. Gutry.

Outstanding Equity Awards at Fiscal 2020 Year-End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2020:

			Option Awards(1)				Stock Awards(1)	
Name	Grant Date	Vesting Commencement Date	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(2)
Josh Lehrer, M.D.	4/20/2020	4/20/2020	—	—	—	—	1,630,407(3)	3,179,294
	5/20/2020	4/20/2020	—	—	—	—	265,414(3)	517,557
Katherine V. Stultz	9/15/2020	8/31/2020	—	—	—	—	505,600(3)(4)	985,920
Philip P. Gutry	10/20/2020	10/5/2020	—	—	—	—	463,433(3)(4)	903,694

(1) Each equity award is subject to the terms of our 2020 Plan.
(2) Based on the fair market value of a share of our common stock on December 31, 2020, which was $1.95.
(3) The shares of restricted stock vest as follows: 25% of the shares on the first anniversary of the vesting commencement date and the remaining 75% in 36 equal monthly installments thereafter, subject to the named executive officer's continuous service relationship with the Company through each applicable vesting date. Notwithstanding the foregoing, if the Company is subject to a Sale Event (as defined in the named executive officer's offer letter) before the named executive officer's service relationship with the Company terminates and the named executive officer's service relationship with the Company is terminated without Cause or for Good Reason (as such terms are defined in the named executive officer's offer letter) within 3 months prior to or 12 months following such Sale Event, then all unvested shares shall immediately vest.
(4) The named executive officer received an early exercisable stock option award, which the named executive officer early exercised in its entirety.

Employee Benefits and Equity Compensation Plans

2020 Stock Option and Grant Plan

On March 24, 2020, our board of directors adopted our Graphite Bio's 2020 Stock Option and Grant Plan (2020 Plan). The 2020 Plan was amended most recently on March 10, 2021. As of December 31, 2020, we reserved an aggregate of 9,974,959 shares of our common stock for the issuance of options and other equity awards under the 2020 Plan. This number is subject to adjustment in the event of a stock split, stock dividend, or other change in our capitalization. As of December 31, 2020, options to purchase 746,000 shares of our common stock at a weighted average exercise price of $0.12 per share and 4,129,815 shares of restricted stock were outstanding under the 2020 Plan and 5,020,152 shares remained available for future issuance under the 2020 Plan. Following this offering, we will not grant any further awards under our 2020 Plan, but all outstanding awards under the 2020 Plan will continue to be governed by their existing terms.

The shares we have issued under the 2020 Plan have been authorized but unissued shares or shares we reacquired. The shares of common stock underlying any awards that are expired, canceled, reacquired by us prior to vesting are currently added back to the shares of common stock available for issuance under the 2020 Plan. Following this offering, such shares will be added to the shares of common stock available for issuance under the 2021 Plan.

The 2020 Plan allows for the grant of incentive stock options to our employees and any of our subsidiary corporations' employees, and for the grant of nonqualified stock options, restricted stock, unrestricted stock, and restricted stock units awards to employees, officers, directors and consultants of us and our subsidiary corporations.

The 2020 Plan is administered by the our board of directors or a committee appointed by it (the plan administrator). The plan administrator has full power to, among other things, select, from among the individuals

eligible for awards, the individuals to whom awards will be granted, to accelerate the time at which a stock award may be exercised or vest, to amend the 2020 Plan and to determine the specific terms and conditions of each award, subject to the provisions of the 2020 Plan.

The plan administrator may exercise its discretion to reduce the exercise price of outstanding stock options under the 2020 Plan or effect repricing through cancellation of such outstanding and by granting such holders new awards in replacement of the cancelled options in accordance with the terms of the 2020 Plan.

Stock options may be granted under our 2020 Plan. The exercise price per share of all stock options must equal at least 100% of the fair market value per share of our common stock on the date of grant. The term of a stock option may not exceed ten years. An incentive stock option granted to a participant who owns more than 10% of the total combined voting power of all classes of our stock on the date of grant, or any subsidiary corporations, may not have a term in excess of five years and must have an exercise price of at least 110% of the fair market value per share of our common stock on the date of grant. The plan administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or certain other property or other consideration acceptable to the plan administrator. After a participant's termination of service, the participant generally may exercise his or her stock options, to the extent vested as of such date of termination, during a period of three months after termination of service. If a termination of service is due to death or disability, the option generally will remain exercisable, to the extent vested as of such date of termination, until the one-year anniversary of such termination of service. However, in no event may an option be exercised later than the expiration of its term. If a termination of service is for cause (as defined in an applicable award agreement), the stock option automatically expires upon the date of the termination of service.

Restricted stock may be granted under our 2020 Plan. Restricted stock awards are grants of shares of our common stock that are subject to various restrictions, including restrictions on transferability and forfeitures provisions. Shares of restricted stock will vest, and the restrictions on such shares will lapse, in accordance with terms and conditions established by the plan administrator.

Unrestricted stock may be granted under our 2020 Plan. Unrestricted stock awards may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

Restricted stock units may be granted under our 2020 Plan. A restricted stock unit is an award that covers a number of shares of our common stock that may be settled upon vesting in cash, by the issuance of the underlying shares or a combination of both. The plan administrator determines the terms and conditions of restricted stock units, including the number of units granted, the vesting criteria (which may include specified performance criteria and/or continued service to us) and the form and timing of payment.

The 2020 Plan generally does not allow for the transfer or assignment of awards, other than, at the discretion of the plan administrator, by gift to an immediate family member, to trusts for the benefit of family members, or to partnerships in which such family members are the only partners, and only the recipient of an award may exercise such an award during his or her lifetime.

In the event of certain changes in our capitalization, the exercise prices of and the number of shares subject to outstanding awards, and the purchase price of and the numbers of shares subject to outstanding awards will be proportionately adjusted, subject to any required action by our Board or stockholders.

The 2020 Plan provides that upon the effectiveness of a "sale event," as defined in the 2020 Plan, an acquirer or successor entity may assume, continue or substitute for the outstanding awards under the 2020 Plan. To the extent that awards granted under the 2020 Plan are not assumed or continued or substituted by acquirer or the successor entity, all stock options and all other awards granted under the 2020 Plan shall terminate. In the event of such termination, individuals holding stock options will be permitted to exercise such options (to the

extent exercisable) prior to the consummation of the sale event. In addition, in connection with the termination of the 2020 Plan upon a sale event, we may make or provide for a cash payment equal to (A) in the case of vested and exercisable options, the difference between (1) the per share cash consideration payable to stockholders (as determined by the plan administrator) in the sale event times the number of shares subject to the options being cancelled and (2) the aggregate exercise price of the options and (B) in the case of restricted stock and restricted stock unit awards, the per share cash consideration payable to stockholders in the sale event multiplied by the number of shares of stock subject to such stock awards (payable at the time of the sale event or upon the later vesting of the awards). In the event of the forfeiture of shares of restricted stock issued under the 2020 Plan, such shares of restricted stock shall be repurchased from the holder at a price per share equal to the lower of (i) the original per share purchase price paid by the recipient of such shares and (ii) the current fair market value of such shares determined immediately prior to the effective time of the sale event. Additionally, our board of directors may resolve, in its sole discretion, to subject any assumed options or payments in respect of options to any escrow, holdback, indemnification, earn-out or similar provisions in the transaction agreements as such provisions apply to holders of our common stock.

Our board of directors may amend, suspend, or terminate the 2020 Plan at any time and for any reason, provided that stockholder approval is obtained where such approval is required by applicable law. Our board of directors has determined not to make any further awards under the 2020 Plan following the completion of this offering.

DIRECTOR COMPENSATION

Compensation to Non-Employee Directors

During the 2020 fiscal year, we did not have a formal director compensation policy, but provided compensation to our independent directors, Messrs. Karsen and Jimenez, in the form of a $25,000 annual cash retainer, pro-rated for the calendar year 2020 based on their respective dates of appointment, payable in monthly installments, and an early exercisable stock option to purchase 252,781 shares of our common stock. The shares underlying the stock options vest in 48 equal monthly installments on the last day of each month over a period of four years beginning on the last day of the month that is the same month on which the director was appointed and are subject to acceleration in full upon a change of control of the Company so long as the individual continues to provide services to us as of such dates. In addition, Mr. Karsen received the following, in connection with his appointment as Chairman of the board of directors effective as of October 28, 2020: (i) a grant of an early exercisable stock option for 126,391 shares of common stock, with the shares underlying the stock option vesting in 48 equal monthly installments on the last day of each calendar month over a period of four years beginning on the last day of the month following the month on which Mr. Karsen was appointed as Chairman of the board of directors, subject to acceleration in full upon a change of control of the Company so long as Mr. Karsen continues to provide services to us as of such dates, and (ii) a $50,000 annual cash retainer, pro-rated for calendar year 2020 based on Mr. Karsen's commencement as Chairman of the board of directors.

We also reimbursed all reasonable out-of-pocket expenses incurred by our directors for their attendance at the meetings of our board of directors or any committee thereof.

Furthermore, in 2020, Dr. Porteus and Dr. Grazia Roncarolo, a former director who resigned from our board of directors in April 2021, received 9,290,000 and 3,000,000 shares of restricted common stock, respectively, as founders of the Company, but not for their services as members of our board of directors.

We intend to adopt a non-employee director compensation policy, pursuant to which our non-employee directors will be eligible to receive compensation for service on our board of directors and committees of our board of directors, to be effective following the completion of this offering.

The following table presents the total compensation for each of our non-employee directors who served as a member of our board of directors during the fiscal year ended December 31, 2020. Dr. Lehrer, who is our Chief Executive Officer, did not receive any additional compensation for his service as a director. The compensation received by Dr. Lehrer, as a named executive officer of the Company, is presented in "Executive Compensation-2020 Summary Compensation Table" above. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity or non-equity awards to or reimburse any expenses of, any of our non-employee directors in 2020.

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)(1)	Option Awards ($)(2)	All Other Compensation ($)	Total ($)
Perry Karsen(3)	18,480	—	298,103	—	312,686
Abraham Bassan(4)	—	—	—	—	—
Jerel Davis, Ph.D.(5)	—	—	—	—	—
Joseph Jimenez(6)	14,483	—	142,187	—	156,670
Matthew Porteus, M.D., Ph.D.(7)	—	42(8)	—	53,846(9)	53,888
Carlo Rizzuto, Ph.D.(10)	—	—	—	—	—
Maria Grazia Roncarolo, M.D., Ph.D.(11)	—	13(12)	—	53,651(13)	53,664

(1) The amounts reported represent the aggregate grant date fair value of the restricted stock awards granted to our directors during the 2020 fiscal year, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the restricted stock awards reported in this column are set

forth in notes 2 and 11 of our financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these restricted stock awards and do not correspond to the actual economic value that may be received by our directors upon the vesting of the restricted stock awards or any sale of the underlying shares of common stock.

(2) The amounts reported represent the aggregate grant date fair value of the stock options granted to our directors during the 2020 fiscal year, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in notes 2 and 11 of our financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these stock options and do not correspond to the actual economic value that may be received by our directors upon the exercise of the stock options or any sale of the underlying shares of common stock.

(3) As of December 31, 2020, Mr. Karsen held 337,043 shares of restricted stock acquired from the early exercise of his options.

(4) As of December 31, 2020, Mr. Bassan did not hold any outstanding equity awards.

(5) As of December 31, 2020, Dr. Davis did not hold any outstanding equity awards.

(6) As of December 31, 2020, Mr. Jimenez held 215,918 shares of restricted stock from the early exercise of his option.

(7) As of December 31, 2020, Dr. Porteus held 8,402,600 shares of founder restricted stock.

(8) Represents the aggregate grant date fair value, calculated in accordance with FASB ASC Topic 718, of Dr. Porteus' founder restricted stock granted on March 24, 2020, which was not granted for service as a member of our board of directors.

(9) Amount represents the advisor fees earned by Dr. Porteus during the fiscal year ended December 31, 2020.

(10) As of December 31, 2020, Mr. Rizzuto did not hold any outstanding equity awards.

(11) As of December 31, 2020, Dr. Grazia Roncarolo held 2,334,450 shares of founder restricted stock.

(12) Represents the aggregate grant date fair value, calculated in accordance with FASB ASC Topic 718, of Dr. Grazia Roncarolo's founder restricted stock granted on March 24, 2020, which was not granted for service as a member of our board of directors.

(13) Amount represents the advisor fees earned by Dr. Grazia Roncarolo during the fiscal year ended December 31, 2020.

Non-Employee Director Advisor Agreements

We have entered into an advisor agreement with each of Drs. Porteus and Grazia Roncarolo, our founders. The material terms of their advisor agreements are summarized below.

Matthew Porteus, M.D., Ph.D.

On March 24, 2020, we entered into an advisory agreement with Dr. Porteus (the Porteus Agreement), pursuant to which he serves on our Scientific & Clinical Advisory Board and among other things, provides consulting services to us involving the development of techniques and improvements in the field of CRISPR, cell and gene therapy and derivatives technologies for the prevention and treatment of human disease, assist us in reviewing goals and developing strategies for achieving such goals, advise on scientific research and support the recruitment of personnel in our research and product development activities. As consideration for such services, Dr. Porteus is entitled to receive an annual retainer of $70,000, subject to his performance of services for nine (9) days per quarter. Furthermore, Dr. Porteus received a restricted stock grant of up to 9,290,000 shares, subject to reduction based on our issuance of common stock to Stanford University, as set forth in the applicable restricted stock purchase agreement. The shares of restricted stock are subject to a four year vesting schedule (up to 25% of the total amount of shares granted (to the extent not previously vested) will vest on June 24, 2021, the first anniversary of the date on which we sold preferred stock with aggregate proceeds of at least $10 million and the remaining 75% vests in equal monthly installments thereafter, subject to continued service through each such date); provided, that 887,400 shares vested on June 10, 2020 upon our execution of a term sheet for a license with Stanford and 100% of the then-unvested shares will vest upon a "change in control" (as defined in the Porteus Agreement) subject to Dr. Porteus remaining in continued service through such date. The Porteus Agreement also provides for reimbursement of travel and out-of-pocket expenses incurred by Dr. Porteus in providing serves at our request, with any expense in excess of $500 per month requiring pre-approval by us. Pursuant to the Porteus Agreement, Dr. Porteus is subject to certain standard assignment of intellectual property and confidentiality covenants, as well as twenty-four (24) month post-termination non-solicitation of employees, consultants and customers restrictive covenants.

Maria Grazia Roncarolo, M.D., Ph.D.

On March 26, 2020, we entered into an advisory agreement with Dr. Grazia Roncarolo (the Grazia Roncarolo Agreement), pursuant to which she serves on our Scientific & Clinical Advisory Board and among

other things, provides consulting services to us involving the development of techniques and improvements in the field of CRISPR, cell and gene therapy and derivatives technologies for the prevention and treatment of human disease, assist us in reviewing goals and developing strategies for achieving such goals, advise on scientific research and support the recruitment of personnel in our research and product development activities. As consideration for such services, Dr. Grazia Roncarolo is entitled to receive an annual retainer of $70,000, subject to her performance of services for six (6) days per quarter. Furthermore, Dr. Grazia Roncarolo received a restricted stock grant of 3,000,000 shares, subject to reduction based on our issuance of common stock to Stanford University, as set forth in the applicable restricted stock purchase agreement. The shares of restricted stock are subject to a four year vesting schedule (up to 25% of the total amount of shares granted (to the extent not previously vested) will vest on June 24, 2021, the first anniversary of the date on which we sold preferred stock with aggregate proceeds of at least $10 million and the remaining 75% vests in equal monthly installments thereafter, subject to continued service through each such date); provided, that 665,550 shares vested on June 10, 2020 upon our execution of a term sheet for a license with Stanford and 100% of the then-unvested shares will vest upon a "change in control" (as defined in the Grazia Roncarolo Agreement) subject to Dr. Grazia Roncarolo remaining in continued service through such date. The Grazia Roncarolo Agreement also provides for reimbursement of travel and out-of-pocket expenses incurred by Dr. Grazia Roncarolo in providing serves at our request, with any expense in excess of $500 per month requiring pre-approval by us. Pursuant to the Grazia Roncarolo Agreement, Dr. Grazia Roncarolo is subject to certain standard assignment of intellectual property and confidentiality covenants, as well as twelve (12) month post-termination non-solicitation of employees, consultants and customers restrictive covenants.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

In addition to the compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections titled "Management" and "Executive and Director Compensation," and the registration rights described in the section titled "Description of Capital Stock—Registration Rights," the following is a description of each transaction to which we were or will be a party, since January 1, 2018:

- the amounts involved exceeded or will exceed $120,000 or one percent of the Company's total assets at year end for the last two completed fiscal years; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, or any affiliated entities, had or will have a direct or indirect material interest.

Private Placements of Securities

Series A Redeemable Convertible Preferred Stock Financing

On June 24, 2020, we sold an aggregate of 15,019,945 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

On December 28, 2020, we sold an additional 15,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

On February 16, 2021, we sold an additional 15,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

All purchasers of our Series A redeemable convertible preferred stock are entitled to specified registration rights. See the section titled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

The following table summarizes the Series A redeemable convertible preferred stock purchased by members of our board of directors or their affiliates and holders of more than 5% of our outstanding capital stock.

Name of Stockholder	Shares of Series A Redeemable Convertible Preferred Stock	Total Purchase Price
Versant Venture Capital VI, L.P.(1)	30,019,945	$ 30,019,945
Samsara BioCapital, L.P.(2)	15,000,000	15,000,000
Total	45,019,945	$ 45,019,945

(1) Versant Venture Capital VI, L.P. (together with its affiliates, Versant Ventures) is a holder of 5% or more of our total outstanding shares, on an as-converted to common stock basis. Jerel Davis, Ph.D. and Carlo Rizzuto, Ph.D., members of our board of directors, are partners at Versant Ventures.

(2) Samsara BioCapital, L.P., together with its affiliates (Samsara BioCapital), is a holder of 5% or more of our total outstanding shares, on an as-converted to common stock basis. Abraham Bassan, a member of our board of directors, is a Vice President at Samsara BioCapital.

Series B Redeemable Convertible Preferred Stock Financing

On March 11, 2021, we sold an aggregate of 29,792,487 shares of our Series B redeemable convertible preferred stock at a purchase price of $5.06 per share, for an aggregate purchase price of approximately $150.7 million.

All purchasers of our Series B redeemable convertible preferred stock are entitled to specified registration rights. See the section titled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

The following table summarizes the Series B redeemable convertible preferred stock purchased by our executive officers, members of our board of directors or their affiliates and holders of more than 5% of our outstanding capital stock.

Name of Stockholder	Shares of Series B Redeemable Convertible Preferred Stock	Total Conversion Price
Versant Vantage II, L.P.(1)	3,715,415	$ 18,799,999.90
Entities affiliated with Samsara BioCapital(2)	1,857,708	9,400,002.48
Perry Karsen(3)	19,763	100,000.78
Joseph Jimenez(3)	19,763	100,000.78
Josh Lehrer, M.D.(3)	19,763	100,000.78
Katherine V. Stultz(4)	19,763	100,000.78
Philip P. Gutry(4)	19,763	100,000.78
Jerry Cacia	19,763	100,000.78
Total	5,691,701	$ 28,800,007.06

(1) Versant Vantage II, L.P. is a holder of 5% or more of our Series B redeemable convertible preferred stock and a holder of 5% or more of our total outstanding shares, on an as-converted to common stock basis. Jerel Davis, Ph.D. and Carlo Rizzuto, Ph.D., members of our board of directors, are partners at Versant Ventures.

(2) Consists of (i) 1,802,372 shares of Series B redeemable convertible preferred stock held by Samsara BioCapital, L.P. and (ii) 55,336 shares of Series B redeemable convertible preferred stock held by 436, L.P. Samsara BioCapital is a holder of 5% or more of our Series B redeemable convertible preferred stock and a holder of 5% or more of our total outstanding shares, on an as-converted to common stock basis. Abraham Bassan, a member of our board of directors, is a Vice President at Samsara Capital.

(3) Each of Perry Karsen, Joseph Jimenez and Josh Lehrer, M.D. are members of our board of directors.

(4) Each of Josh Lehrer, M.D., Katherine V. Stultz, Philip P. Gutry and Jerry Cacia are our executive officers.

Agreements with Stockholders

Investors' Rights Agreement

On March 11, 2021, we entered into an Amended and Restated Investors' Rights Agreement, as amended to date, which we refer to as our investors' rights agreement, with certain holders of our outstanding redeemable convertible preferred stock, including entities with which certain of our directors are affiliated. After the completion of this offering, the holders of shares of our common stock issuable in connection with the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into common stock, are entitled to rights with respect to the registration of their shares following this offering under the Securities Act. See the section titled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

Right of First Refusal and Co-Sale Agreement

On March 11, 2021, we entered into an Amended and Restated Right of First Refusal and Co-Sale Agreement, as amended to date, which we refer to as our right of first refusal and co-sale agreement, which

imposes restrictions on the transfer of our capital stock. Upon the completion of this offering, the right of first refusal and co-sale agreement will terminate and the restrictions on the transfer of our capital stock set forth in this agreement will no longer apply.

Voting Agreement

On March 11, 2021, we entered into an Amended and Restated Voting Agreement, as amended to date, which we refer to as our voting agreement, under which certain holders of our capital stock, including persons who hold more than 5% of our outstanding capital stock and entities with which certain of our directors are affiliated, have agreed to vote their shares on certain matters, including with respect to the election of directors. Upon the completion of this offering, the voting agreement will terminate and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors or the voting of our capital stock of the company.

Executive Officer and Director Compensation

See the sections titled "Executive Compensation" and "Director Compensation" for information regarding compensation of our executive officers and directors.

Indemnification Agreements

In connection with this offering, we intend to enter into new agreements to indemnify our directors and executive officers. These agreements and our amended and restated certificate of incorporation and amended and restated bylaws will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our Company or that person's status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Prior to this offering, we have not had a formal policy regarding approval of transactions with related parties. Prior to the completion of this offering, we expect to adopt a written related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy will become effective immediately upon the execution of the underwriting agreement for this offering. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were, or will be participants and in which the amount involved exceeds $120,000 or one percent of the Company's total assets at year end for the last two completed fiscal years. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person is any executive officer, director, or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors, for review, consideration, and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction, and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer, and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related person transactions and to effectuate the terms of the policy.

In addition, under our Code of Conduct, which we intend to adopt in connection with this offering, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

In considering related person transactions, our audit committee, or other independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs, and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director, or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify, or reject a related person transaction, our audit committee, or other independent body of our board of directors, must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our stockholders, as our audit committee, or other independent body of our board of directors, determines in the good faith exercise of its discretion. All of the transactions described above were entered into prior to the adoption of the written policy, but all were approved by our board of directors considering similar factors to those described above.

PRINCIPAL STOCKHOLDERS

The following table presents information concerning the beneficial ownership of the shares of our common stock as of April 15, 2021 by:

- each person we know to be the beneficial owner of 5% or more of our outstanding shares of our capital stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with SEC rules. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, a person is deemed to be a beneficial owner of our common stock if that person has a right to acquire ownership within 60 days by the exercise of options or the conversion of our redeemable convertible preferred stock. A person is also deemed to be a beneficial owner of our common stock if that person has or shares voting power, which includes the power to vote or direct the voting of our common stock, or investment power, which includes the power to dispose of or to direct the disposition of such capital stock. Except in cases where community property laws apply or as indicated in the footnotes to this table, we believe that each stockholder identified in the table possesses sole voting and investment power over all shares of common stock shown as beneficially owned by the stockholder.

Percentage of beneficial ownership in the table below is based on 102,045,839 shares of common stock deemed to be outstanding as of April 15, 2021, assuming the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into common stock, immediately prior to the completion of this offering. The table below assumes that the underwriters do not exercise their over-allotment option. Shares of common stock subject to options that are currently exercisable or exercisable within 60 days of April 15, 2021 are considered outstanding and beneficially owned by the person holding the options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated below, the address of each individual listed below is c/o Graphite Bio, Inc., 279 East Grand Avenue, Suite 430, South San Francisco, CA 94080.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned Before Offering	Percentage of Shares Beneficially Owned After Offering
5% or Greater Stockholders:			
Entities Affiliated with Versant Ventures		%	%
Entities Affiliated with Samsara BioCapital		%	%
Matthew Porteus, M.D., Ph.D.		%	%
Named Executive Officers and Directors:			
Josh Lehrer, M.D.		%	%
Katherine V. Stultz		%	%
Philip P. Gutry		%	%
Perry Karsen		%	%
Abraham Bassan		%	%
Jerel Davis, Ph.D.		%	%
Kristen M. Hege, M.D.		%	%
Joseph Jimenez		%	%
Matthew Porteus, M.D., Ph.D.		%	%
Carlo Rizzuto, Ph.D.		%	%
Smital Shah		%	%
Jo Viney, Ph.D.		%	%
All executive officers and directors as a group (13 persons)		%	%

* Represents beneficial ownership of less than one percent.

DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering, our authorized capital stock will consist of shares of common stock, par value $0.00001 per share, and shares of preferred stock, par value $0.00001 per share, all of which will be undesignated, and there will be shares of common stock outstanding and no shares of preferred stock outstanding. As of March 31, 2021, we had approximately 52 record holders of our capital stock. All of our outstanding shares of redeemable convertible preferred stock will convert into shares of our common stock immediately prior to the completion of this offering. In addition, upon the completion of this offering, options to purchase shares of our common stock will be outstanding and shares of our common stock will be reserved for future grants under our equity incentive plans.

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and bylaws are summaries of material terms and provisions and are qualified by reference to our amended and restated certificate of incorporation and bylaws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part. The descriptions of our common stock and preferred stock reflect amendments to our amended and restated certificate of incorporation and bylaws that will become effective immediately prior to the completion of this offering.

Common Stock

Upon the completion of this offering, we will be authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Except as described under "Anti-Takeover Effects of Delaware Law and Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws" below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and bylaws. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights and no sinking fund provisions are applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Convertible Preferred Stock

Immediately prior to completion of this offering, all outstanding shares of our redeemable convertible preferred stock will be converted into shares of our common stock. Upon the completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our Company, which might harm the market price of our common stock. See also "—Anti-Takeover Effects of Delaware Law and Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws—Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws—Undesignated Preferred Stock" below.

Our board of directors will make any determination to issue such shares based on its judgment as to our Company's best interests and the best interests of our stockholders. Upon the completion of this offering, we will have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

Options

As of December 31, 2020, we had outstanding options to purchase 746,000 shares of our common stock, with a per share weighted-average exercise price of $0.12 under our 2020 Plan.

Registration Rights

Upon the completion of this offering, the holders of shares of our common stock, including shares issuable upon the automatic conversion of our redeemable convertible preferred stock, or their permitted transferees, which we refer to as our registrable securities, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the investor rights agreement. The investor rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses incurred in connection with registrations under the investor rights agreement will be borne by us, and all selling expenses, including estimated underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning 180 days after the effective date of this registration statement, the holders of our registrable securities are entitled to demand registration rights. Under the terms of our investor rights agreement, we will be required, upon the request of holders of at least a majority of our outstanding registrable securities, to file a registration statement and use commercially reasonable efforts to effect the registration of these shares for public resale. We are required to effect up to two registrations pursuant to this provision of the investor rights agreement.

Short-Form Registration Rights

Upon the completion of this offering, the holders of our registrable securities are also entitled to short form registration rights. Pursuant to our investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the request of holders of at least 20% of our outstanding registrable securities to sell registrable securities with an anticipated aggregate offering amount of at least $5.0 million net of certain expenses related to the offering, we will be required to use our commercially reasonable efforts to effect a registration of such shares. We are required to effect up to two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

Piggyback Registration Rights

The holders of our registrable securities are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration. Subject to certain exceptions contained in the investor rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters determine that marketing factors require a limitation of the number of shares to be underwritten.

Indemnification

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expenses of Registration

We will pay the registration expenses, subject to certain limited exceptions contained in the investor rights agreement, of the holders of the shares registered pursuant to the demand, short form and piggyback registration rights described above, including the expenses of one counsel for the selling holders.

Expiration of Registration Rights

The registration rights granted under the investor rights agreement will terminate upon the earlier of (i) a deemed liquidation event, as defined in our amended and restated certificate of incorporation (as in effect prior to the completion of this offering) or certain other events constituting a sale of the company, (ii) at such time after our initial public offering when all registrable securities could be sold under Rule 144 of the Securities Act or a similar exemption without limitation during a three-month period without registration or (iii) the fifth anniversary of our initial public offering.

Anti-Takeover Effects of Delaware Law and Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Certain provisions of the Delaware General Corporation Law and of our amended and restated certificate of incorporation and bylaws that will become effective immediately prior to the completion of this offering could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Takeover Statute

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and bylaws to be in effect immediately prior to completion of this offering will include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies. In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders. Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholder without holding a meeting of stockholders.

Meetings of stockholders. Our bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements. Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our bylaws.

Amendment to certificate of incorporation and bylaws. As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our amended and restated certificate of incorporation must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority vote of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock. Our amended and restated certificate of incorporation provides for authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors' broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive forum. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for: (i) any derivative action or proceeding brought on behalf of our Company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to the company or our stockholders, (iii) any action asserting a claim against our Company arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws, (iv) any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or (v) any action asserting a claim against our Company governed by the internal affairs doctrine. This exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. In addition, unless we consent in writing to the selection of an alternate forum, the United States District Courts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Although our amended and restated bylaws contain the choice of forum provision described above, it is possible that a court could rule that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is . The transfer agent and registrar's address is .

Listing

We intend to apply to list our common stock on the Nasdaq Global Market under the symbol "GRPH."

Limitations of Liability and Indemnification Matters

For a discussion of liability and indemnification, see the section titled "Management—Limitation on Liability and Indemnification Matters."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Sale of Restricted Shares

Based on the number of shares of common stock outstanding as of December 31, 2020, upon completion of this offering, shares of common stock will be outstanding, assuming no exercise by the underwriters of their over-allotment option and no exercise of options. All of the shares sold in this offering will be freely tradable. The remaining shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below. Following the expiration of the lock-up period, all shares will be eligible for resale in compliance with Rule 144 or Rule 701 under the Securities Act. "Restricted securities" as defined under Rule 144 of the Securities Act were issued and sold by us in reliance on exemptions from the registration requirements of the Securities Act. These shares may be sold in the public market only if registered or qualified for an exemption from registration, such as under Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately shares immediately after this offering assuming no exercise of the underwriters' over-allotment option, based on the number of shares outstanding as of December 31, 2020; or
- the average weekly trading volume of our common stock on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act (Rule 701), as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under the section titled "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-up Agreements

In connection with this offering, we, each of our directors and executive officers, and holders of substantially all of our securities have agreed with the underwriters that for a period of 180 days following the date of this prospectus, among other things and subject to certain exceptions, we and they will not offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock. The representatives of the underwriters may, in their sole discretion, at any time, release all or any portion of the shares from the restrictions in that agreement.

Rule 10b5-1 Trading Plans

Following the completion of this offering, certain of our officers, directors and significant stockholders may adopt written plans, known as Rule 10b5-1 trading plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the officer, director or stockholder when entering into the plan, without further direction from such officer, director or stockholder. Such sales would not commence until the expiration of the applicable lock-up agreements entered into by such officer, director or stockholder in connection with this offering.

Registration Rights

We are party to an investor rights agreement which provides that holders holding shares of our common stock, including shares issuable upon the automatic conversion of our redeemable convertible preferred stock, have the right to demand that we file a registration statement or request that their shares of our common stock be covered by a registration statement that we are otherwise filing. See the section titled "Description of Capital Stock—Registration Rights" in this prospectus. Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon effectiveness of the registration, subject to the expiration of the lock-up period described above and under the section titled "Underwriting" in this prospectus, and to the extent such shares have been released from any repurchase option that we may hold.

Equity Incentive Plans

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options and other equity awards outstanding or reserved for issuance under our equity incentive plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements. For a more complete discussion of our equity incentive plans, see the section titled "Executive and Director Compensation—Employee Benefits and Stock Plans."

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TONON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax considerations applicable tonon-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that arepass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or an investor in any other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the Internal Revenue Code of 1986 as amended (the Code), existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particulamon-U.S. holder in light of that non-U.S. holder's individual circumstances including the alternative minimum tax, or the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code and any election to apply Section 1400Z-2 of the Code to gains recognized with respect to shares of our common stock. This discussion also does not address any U.S. state, local or non-U.S. taxes or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);

- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- persons who have elected to mark securities to market;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- certain U.S. expatriates; and
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the common stock being taken into account in an applicable financial statement under Section 451(b) of the Code.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale of Other Taxable Disposition of our Common Stock." Any such distributions will also be subject to the discussions below under the sections titled "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. If we or another withholding agent apply over-withholding or if a non-U.S. holder does not timely provide us with the required certification, the non-U.S. holder may be entitled to a refund or credit of any excess tax withheld by timely filing an appropriate claim with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under sections titled "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale of other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market, within the meaning of the relevant provisions of the Code, and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of

information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act (FATCA), generally imposes a U.S. federal withholding tax at a rate of 30% on certain types of payments made to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA currently applies to payments of dividends on our common stock. Currently proposed U.S. Treasury Regulations provide that FATCA withholding does not apply to gross proceeds from the disposition of property of a type that can produce U.S. source dividends or interest; however, prior versions of the rules would have made such gross proceeds subject to FATCA withholding. Taxpayers (including withholding agents) can currently rely on the proposed Treasury Regulations. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC, BofA Securities, Inc., Cowen and Company, LLC and SVB Leerink LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	
BofA Securities, Inc.	
Cowen and Company, LLC	
SVB Leerink LLC	
Total	

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below. The offering of the shares of common stock by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $ per share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an over-allotment option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares of common stock at the public offering price listed on the cover page of this prospectus, less estimated underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the over-allotment option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' over-allotment option to purchase up to an additional shares of our common stock.

		Total	
	Per Share	No Exercise	Full Exercise
Public offering price	$	$	$
Underwriting discounts and commissions to be paid by us	$	$	$
Proceeds, before expenses, to us	$	$	$

The estimated offering expenses payable by us, exclusive of the estimated underwriting discounts and commissions, are approximately $. We have also agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority up to $.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

We intend to apply to list our common stock on the Nasdaq Global Market under the trading symbol "GRPH."

We and all of our directors and officers and the holders of substantially all of our outstanding securities have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, BofA Securities, Inc., Cowen and Company, LLC and SVB Leerink LLC on behalf of the underwriters, we and they will not, and will not publicly disclose an intention to, during the period ending 180 days after the date of this prospectus (the restricted period):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock; or
- enter into any hedging, swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, BofA Securities, Inc., Cowen and Company, LLC and SVB Leerink LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply, among other things and subject to certain exceptions, to:

- transactions relating to shares of our common stock or other securities acquired in this offering and in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions;
- transfers of our securities as a bona fide gift or gifts;
- transfers of our securities to an immediate family member or trust for the direct or indirect benefit of the securityholder or an immediate family member;
- distributions of our securities to any general or limited partners, members, beneficiaries or other equity holders of the securityholder or to any investment fund or other entity that controls, manages, is controlled by, or is under common control with the securityholder;
- transfers of our securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the securityholder or by operation of law pursuant to order of a court in connection with a divorce settlement or a domestic relations order, provided that each transferee, donee or distributee signs a lock-up agreement and no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such transfer;
- transfers or dispositions of our securities pursuant to any contractual arrangement in effect on the date of this prospectus and disclosed in this prospectus that provides for the repurchase of shares of

common stock in connection with the termination of the securityholder's employment with or service to us, provided, that no public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period within 75 days after the date the securityholder ceases to provide services to us, and after such 75th day, if the securityholder is required to file a report reporting a reduction in beneficial ownership of shares of common stock during the restricted period, such report or filing shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this clause and no public filing, report or announcement shall be voluntarily made;

- conversion of any outstanding shares of preferred stock or other securities described in this prospectus and outstanding as of the date of this prospectus into shares of common stock, provided that any such securities received upon such conversion shall be subject to the terms of the lock-up agreement and that no filing under Section 16(a) of the Exchange Act or other public filing, report or announcement shall be voluntarily made and, if any filing under Section 16(a) of the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock in connection with such transfer or distribution shall be legally required during the restricted period, the securityholder shall clearly indicate in the footnotes thereto the nature and conditions of such transfer;

- transfers to us in connection with the "net" or "cashless" exercise or settlement solely to cover withholding tax obligations in connection with the exercise or settlement of such warrants or stock options, restricted stock units or other equity awards expiring during the restricted period, in each case pursuant to a stock incentive plan, other equity award plan or warrant described in this prospectus, provided no public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period within 60 days after the date of this prospectus, and after such 60th day, if the securityholder is required to file a report reporting a reduction in beneficial ownership of shares of common stock during the restricted period, such report or filing shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this clause and that the shares of common stock received upon exercise of the stock option or warrant or vesting event are subject to the lock-up agreement, and no public filing, report or announcement shall be voluntarily made;

- the establishment of a trading plan on behalf of a securityholder, officer, or director of our Company pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that such plan does not provide for the transfer of common stock during the restricted period and if any public announcement or filing under the Exchange Act is required of or voluntarily made by or on behalf of the securityholder or us regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period;

- transfers of our securities pursuant to a bona fide third-party tender offer, merger, consolidation, business combination, stock purchase or other similar transaction or series of related transactions approved by our board of directors and made to all holders of our common stock involving a change in control, provided that in the event that such transaction or series of related transactions is not completed, the securityholder shall remain subject to the restrictions set forth in the lock-up agreement with respect to the securityholder's shares of common stock and any security convertible into or exercisable or exchangeable for common stock;

- transfers by our founders to us in connection with the repurchase by us of common stock pursuant to the Stanford Adjustment Repurchase Right and a stock purchase agreement, provided it shall be a condition to such transfer that no filing under Section 16(a) of the Exchange Act or other public filing, report or announcement shall be voluntarily made and, if any filing, report or announcement shall be required, such filing, report or announcement shall clearly indicate in the footnotes thereto the nature and conditions of such transfer; or

- transfers of our securities to the underwriters or otherwise with the consent of Morgan Stanley & Co. LLC, BofA Securities, Inc., Cowen and Company, LLC and SVB Leerink LLC.

Morgan Stanley & Co. LLC, BofA Securities, Inc., Cowen and Company, LLC and SVB Leerink LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in

determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

Selling Restrictions

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of anon-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area (each a Relevant State), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the shares may be offered to the public in that Relevant State at any time:

(i) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;

(ii) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or

(iii) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the shares shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to the shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

United Kingdom

No shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the Shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

(i) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

(ii) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or

(iii) in any other circumstances falling within Section 86 of the FSMA,

provided that no such offer of the shares shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Hong Kong

Shares of our common stock may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong); (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder; or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to shares of our common stock may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) (the FIEL) has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors (QII)

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a "QII only private placement" or a "QII only secondary distribution" (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a "small number private placement" or a "small number private secondary distribution" (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares of our common stock may not be circulated or distributed, nor may the shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA); (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where shares of our common stock are subscribed or purchased under Section 275 by a relevant person which is: (i) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (ii) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired shares of our common stock under Section 275 except: (a) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (b) where no consideration is given for the transfer; or (c) by operation of law.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX), or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market

Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (DFSA). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001(Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (Exempt Investors), who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the Addressed Investors); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the Qualified Investors). The Qualified Investors shall not be taken into account in

the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Goodwin Procter LLP, San Francisco, California. Legal matters in connection with the offering will be passed upon for the underwriters by Cooley LLP, San Diego, California.

EXPERTS

The financial statements included in this registration statement have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements and financial statement schedules are included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock being offered by this prospectus, which constitutes a part of the registration statement. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. Upon completion of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available via the SEC's website at www.sec.gov. We also maintain a website at https://graphitebio.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. However, the information contained in or accessible through our website is not part of this prospectus or the registration statement of which this prospectus forms a part, and investors should not rely on such information in making a decision to purchase our common stock in this offering.

Graphite Bio, Inc.
INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Graphite Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Graphite Bio, Inc. (the "Company") as of December 31, 2019 and 2020, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows, for the years then ended, 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, 2019 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, 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 and in accordance with auditing standards generally accepted in the United States of America. 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

San Francisco, California
April 16, 2021

We have served as the Company's auditor since 2021.

Graphite Bio, Inc.
Balance Sheets
(in thousands, except share and per share data)

	As of December 31,	
	2019	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 6	$ 19,782
Restricted cash	—	35
Prepaid expenses and other current assets	—	1,286
Total current assets	6	21,103
Property and equipment, net	—	1,461
Total assets	$ 6	$ 22,564
Liabilities, redeemable convertible preferred stock, and stockholders' deficit		
Current liabilities:		
Accounts payable	$ —	$ 630
Accrued compensation	—	466
Accrued expenses	19	1,890
Redeemable convertible preferred stock tranche liability	—	29,062
Related party convertible note	2,205	—
Total current liabilities	2,224	32,048
Other liabilities	—	316
Total liabilities	2,224	32,364
Commitments and contingencies (Note 7)		
Redeemable convertible preferred stock, $0.00001 par value; 45,024,986 shares authorized, 30,019,945 shares issued and outstanding; liquidation preference $30,020 as of December 31, 2020	—	55,608
Stockholders' deficit:		
Common stock, $0.001 par value: 1,000 shares authorized and 1 share issued and outstanding as of December 31, 2019; $0.00001 par value: 80,000,000 shares authorized and 24,998,807 shares issued and outstanding as of December 31, 2020	—	—
Additional paid-in capital	—	5,183
Accumulated deficit	(2,218)	(70,591)
Total stockholders' deficit	(2,218)	(65,408)
Total liabilities, redeemable convertible preferred stock, and stockholders' deficit	$ 6	$ 22,564

The accompanying notes are an integral part of these financial statements.

Graphite Bio, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2019	2020
Operating expenses:		
Research and development	$ —	$ 9,123
General and administrative	29	4,377
Total operating expenses	29	13,500
Loss from operations	(29)	(13,500)
Other income (expense), net:		
Related party convertible note interest expense	(80)	(40)
Change in fair value of the redeemable convertible preferred stock tranche liabilities	—	(54,833)
Total other income (expense), net	(80)	(54,873)
Net loss and comprehensive loss	$ (109)	$ (68,373)
Net loss per share attributable to common stockholders—basic and diluted	$ (109,000)	$ (12.31)
Weighted-average shares used in computing net loss per share—basic and diluted	1	5,554,899

The accompanying notes are an integral part of these financial statements.

Graphite Bio, Inc.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share data)

	Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balance as of December 31, 2018	—	$ —	1	$ —	$ —	$ (2,109)	$ (2,109)
Net loss	—	—	—	—	$ —	(109)	(109)
Balance as of December 31, 2019	—	$ —	1	$ —	—	$ (2,218)	$ (2,218)
Common shares issued to founders and investor	—	—	20,789,999	—	—	—	—
Issuance of restricted common shares	—	—	2,025,821	—	—	—	—
Issuance of redeemable convertible preferred stock upon conversion of outstanding related party convertible note and accrued interest	5,019,945	5,020	—	—	—	—	—
Related party convertible note and accrued interest cancellation	—	—	—	—	2,225	—	2,225
Issuance of redeemable convertible preferred stock for cash, net of issuance costs of $ 184 and fair value of tranche liability of $ 3,329	25,000,000	21,488	—	—	—	—	—
Stock based compensation expense	—	—	—	—	177	—	177
Common stock shares issued upon early exercise of options	—	—	2,182,986	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	9	—	9
Reclassification of tranche liability upon settlement	—	29,100	—	—	—	—	—
Obligation to issue common stock shares for license	—	—	—	—	2,772	—	2,772
Net loss	—	—	—	—	—	(68,373)	(68,373)
Balance as of December 31, 2020	30,019,945	$ 55,608	24,998,807	$ —	$ 5,183	$ (70,591)	$ (65,408)

The accompanying notes are an integral part of these financial statements

Graphite Bio, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2019	2020
Cash flows from operating activities:		
Net loss	$ (109)	$ (68,373)
Adjustments to reconcile net loss to net cash used by operations:		
Depreciation	—	121
Interest expense related to convertible notes	80	40
Stock based compensation expense	—	177
Change in fair value of the redeemable convertible preferred stock tranche liability	—	54,833
R&D expense incurred to issue common stock to Stanford	—	2,772
Changes in assets and liabilities:		
Prepaid expenses and other current assets	7	(1,286)
Accounts payable	(12)	594
Accrued compensation	—	466
Accrued expenses	15	1,871
Other liabilities	—	64
Net cash used in operating activities	(19)	(8,721)
Cash flows from investing activities:		
Purchases of property, plant and equipment	—	(1,545)
Net cash used in investing activities	—	(1,545)
Cash flows from financing activities:		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	24,816
Proceeds from issuance of related party convertible note	—	5,000
Proceeds from issuance of common stock shares upon early exercises of stock options and restricted stock shares	—	261
Net cash provided by financing activities	—	30,077
Net (decrease) increase in cash, cash equivalents and restricted cash	(19)	19,811
Cash, cash equivalents and restricted cash, at beginning of period	25	6
Cash, cash equivalents and restricted cash, at end of period	$ 6	$ 19,817
Reconciliation of cash, cash equivalents and restricted cash to statement of financial position:		
Cash and cash equivalents	$ 6	$ 19,782
Restricted cash	—	35
Cash, cash equivalents and restricted cash in statement of financial position	$ 6	$ 19,817
Supplemental disclosures of non-cash investing and financing information:		
Related party convertible note and accrued interest cancellation	—	(2,225)
Issuance of redeemable convertible preferred stock upon conversion of outstanding related party convertible note and accrued interest	—	5,020
Purchases of propery, plant and equipment included in accounts payable	—	(35)
Vesting of early exercised stock options	—	9
Settlement of redeemable convertible preferred stock tranche liability	—	$ (29,100)

The accompanying notes are an integral part of these financial statements.

Graphite Bio, Inc.
Notes to Financial Statements

1. Description of Business, Organization and Liquidity

Organization and Business

Graphite Bio, Inc. (the "Company") is a clinical-stage, next-generation gene editing company harnessing high efficiency targeted gene integration to develop a new class of therapies to potentially cure a wide range of serious and life-threatening diseases. The Company is pioneering a precision gene editing approach to achieve one of medicine's most elusive goals: to precisely "find & replace" any gene in the genome. The Company's next-generation gene editing platform allows us to precisely correct mutations, replace entire disease-causing genes with normal genes, or insert new genes into predetermined, safe locations. The Company's lead product candidate GPH101 is a highly differentiated approach with the potential to directly correct the mutation that causes sickle cell disease (SCD) and restore normal adult hemoglobin (HgbA) expression. The Company has received clearance of its IND application and intends to enroll the first patient in a Phase 1/2 clinical trial.

From its inception in 2017, the Company's primary activities have been to perform research and development, undertake preclinical studies and enable manufacturing activities in support of its product development efforts, organize and staff the Company, establish its intellectual property portfolio, and raise capital to support and expand such activities.

The Company was incorporated in Ontario, Canada in June 2017 as Longbow Therapeutics Inc., and was reincorporated in the State of Delaware in October 2019. In February 2020, the Company changed its name to Integral Medicines, Inc., and again in August 2020, changed the name to Graphite Bio, Inc. Research and development of the Company's initial technology ceased at the end of 2018, and the Company did not have any significant operations or any research and development activities in 2019. In March 2020, the Company identified new gene editing technology which the Company sought to further develop, and the Company licensed the related intellectual property from The Board of Trustees of the Leland Stanford Junior University ("Stanford") in December 2020 (Note 6).

Liquidity

The Company has incurred significant operating losses since inception and has primarily relied on private equity and convertible debt financings to fund its operations. As of December 31, 2020, the Company had an accumulated deficit of $70.6 million, of which $54.8 million related to the change in fair value of the redeemable convertible preferred stock tranche liabilities. The Company expects to continue to incur substantial losses, and its transition to profitability will depend on the successful development, approval and commercialization of product candidates and on the achievement of sufficient revenues to support its cost structure. The Company may never achieve profitability, and unless and until then, the Company will need to continue to raise additional capital. Management expects that the existing cash of $19.8 million as of December 31, 2020, $15.0 million cash received in connection with the closing of the third tranche of Series A preferred stock financing in March 2021 and $150.7 million cash received in March 2021 in connection with the Series B preferred stock financing will be sufficient to fund its current operating plan for at least the next 12 months from the date of issuance of these financial statements.

Coronavirus Pandemic

In March 2020, the World Health Organization declared the global novel coronavirus disease 2019("COVID-19"), outbreak a pandemic. The ongoing COVID-19 pandemic may continue to affect the Company's ability to initiate and complete preclinical studies, delay the initiation of its planned clinical trials or future clinical trials or the progress or completion of its ongoing clinical trials, impede regulatory activities, disrupt the supply chain and the manufacture or shipment of drug substances and finished drug products for its product candidates for use in its clinical trials, impair testing, monitoring, data collection and analysis and other related activities or have other adverse effects on the Company's business, financial condition, results of operations and

prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on the Company's business and operations and its ability to raise additional funds to support our operations.

The Company is following, and will continue to follow, recommendations from the U.S. Centers for Disease Control and Prevention as well as federal, state, and local governments regarding working-from-home practices for non-essential employees as well as return-to-work policies and procedures. The Company expects to continue to take actions as may be required or recommended by government authorities or as the Company determines are in the best interests of its employees and other business partners in light of the pandemic.

In light of the ongoing COVID-19 pandemic, the Company's partner Stanford was delayed in making an IND-filing. While the Company's operations to date have not been significantly impacted by the COVID-19 pandemic, it cannot at this time predict the specific extent, duration, or full impact that the COVID-19 pandemic will have on its business, financial condition and operations, including planned clinical trials and clinical development timelines, The impact of the COVID-19 pandemic on the Company's financial performance will depend on future developments, including the duration and spread of the pandemic, its impact on the Company's clinical trial enrollment, trial sites, contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and other third parties with whom it does business, its impact on regulatory authorities and the Company's key scientific and management personnel, progress of vaccination and related governmental advisories and restrictions. These developments and the impact of the COVID-19 pandemic on the financial markets and the overall economy are highly uncertain and cannot be predicted. If the financial markets or the overall economy are impacted for an extended period, the Company's business may be materially adversely affected.

2. Summary of Significant Accounting Policies

Basis of Presentation

These financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

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 and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of expenses during the reporting period. On an ongoing basis, the Company evaluates estimates and assumptions, including but are not limited to those related to the fair value of a derivative redeemable convertible preferred stock tranche liabilities, the fair value of redeemable convertible preferred stock and common stock, stock-based compensation expense, accruals for research and development costs, the valuation of deferred tax assets, and uncertain income tax positions. Management bases its estimates on historical experience and on various other assumptions that are believed to be 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. Actual results may differ materially from those estimates.

Concentration of Credit Risk

Cash and cash equivalents are financial instruments that potentially subject the Company to concentrations of credit risk. Substantially all of the Company's cash and cash equivalents are deposited in accounts with major financial institution and amounts may exceed federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial strength of the depository institution in which the cash and cash equivalents are held. The Company has not experienced any losses on deposits of cash and cash equivalents.

Graphite Bio, Inc.
Notes to Financial Statements

Risks and Uncertainties

The Company is subject to certain risks and uncertainties, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on the future financial position or results of operations: the timing of, and the Company's ability to advance its current and future product candidates into and through clinical development; costs and timelines associated with the manufacture of clinical supplies of the Company's product candidates; regulatory approval and market acceptance of, and reimbursement for its product candidates; performance of third-party CROs and CMOs; competition from pharmaceutical companies with greater financial resources or expertise; protection of the intellectual property; litigation or claims against the Company based on intellectual property or other factors; and its ability to attract and retain employees necessary to support its growth. Disruption from CROs', CMOs' or suppliers' operations would likely have a negative impact on the Company's business, financial position and results of operations.

Segment and Geographical Information

The Company operates and manages its business as one reportable and operating segment. The chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. All of the Company's long-lived assets are based in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with a maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2019, and 2020, cash and cash equivalents consisted of cash and money market funds.

Restricted Cash

Restricted cash of $34,870 as of December 31, 2020 represented a security deposit in the form of a letter of credit issued in connection with the lease of the Company's headquarters (Note 7).

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly relatedto in-process equity financings, including the planned initial public offering of its common stock (the "IPO"), until such financings are consummated. After consummation of the IPO, these costs are recorded as a reduction of the proceeds received as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be immediately recognized as operating expenses. No deferred offering costs were capitalized as of December 31, 2019 and 2020.

Property and Equipment, Net

Property and equipment are recorded at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally three to five years. Repairs and maintenance expenditures, which are not considered improvements and do not extend the useful life of property and equipment, are expensed as incurred. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in the statements of operations and comprehensive loss in the period realized.

Graphite Bio, Inc.
Notes to Financial Statements

Asset Acquisitions

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire in-process research and development ("IPR&D") with no alternative future use is charged to research and development expense at the acquisition date. Please refer to Note 6 for more details on asset acquisition.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future undiscounted net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows generated by the assets. There have been no such impairments of long-lived assets in the years ended December 31, 2019 and 2020.

Redeemable Convertible Preferred Stock

The Company records shares of redeemable convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. The redeemable convertible preferred stock is recorded outside of permanent equity because while it is not mandatorily redeemable, redemption is contingent upon the occurrence of certain events considered not solely within the Company's control. The Company has not adjusted the carrying values of the redeemable convertible preferred stock to the liquidation preferences of such shares because it is uncertain whether or when a deemed liquidation event would occur that would obligate the Company to pay the liquidation preferences to holders of shares of redeemable convertible preferred stock. Subsequent adjustments to the carrying values to the liquidation preferences will be made only when it becomes probable that such a deemed liquidation event will occur.

Redeemable Convertible Preferred Stock Tranche Liabilities

The Company has determined that its obligation to issue additional shares of redeemable convertible preferred stock upon the occurrence of certain events or the Company's Board of Directors (the "Board") consent represents a freestanding financial instrument. The instrument is classified as a liability on the balance sheets and is subject to re- measurement at each balance sheet date and at the settlement date, any change in fair value is recognized through other income (expense) in the statements of operations and comprehensive loss.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of financial instruments, including restricted cash, prepaid expenses and other current assets, accounts payable, accrued compensation, accrued expenses, and other liabilities, approximate fair value due to their short-term maturities. The cash invested in money-market funds and redeemable convertible preferred stock tranche liability are carried at fair value.

Graphite Bio, Inc.
Notes to Financial Statements

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs include salaries, stock-based compensation, and benefits for employees performing research and development activities, an allocation of facility and overhead expenses, expenses incurred under agreements with consultants, CMOs, CROs and investigative sites that conduct preclinical studies, other supplies and costs associated with product development efforts, preclinical activities, and regulatory operations.

Accrued Research and Development Expenses

The Company has entered into various agreements with outsourced vendors, CROs and CMOs. Research and development accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses on the balance sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered. To date, there have been no material differences between estimates of such expenses and the amounts actually incurred.

Tax Credit Receivable

The Company is eligible for federal and California research and development credits for its research and development activities performed within the United States and California, respectively. The credits are, generally, available to offset federal and California income tax liabilities as applicable. The Company has applied $0.2 million of federal research and development credits to offset its federal payroll tax expenses for the year ended December 31, 2020 due to its small business status. The Company is electing to utilize $250,000 of current year R&D credit generated against the employer portion of the payroll tax.

Income Taxes

The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover deferred income tax assets, the Company considers all available positive and negative evidence, including operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize deferred income tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2019, and 2020, the Company has recorded a full valuation allowance on deferred tax assets.

On March 27, 2020, the President of the United States signed into law the Coronavirus Aid, Relief, and Economic Security Act (CARES Act). The CARES Act, among other things, includes certain income tax provisions for individual and corporations; however, these benefits do not impact current tax provision.

Graphite Bio, Inc.
Notes to Financial Statements

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Stock-Based Compensation Expense

The Company's stock-based equity awards include restricted stock awards and stock options that are granted to employees and consultants that are accounted at fair value on the award grant date. Stock-based compensation expense is recognized over the awards' vesting period on a straight-line basis and recorded as either research and development or general and administrative expenses in the statements of operations and comprehensive loss based on the function to which the related services are provided. Forfeitures are accounted for as they occur.

The Black-Scholes option-pricing model, used to estimate fair value of stock-based awards, requires the use of the following assumptions:

- *Expected term*—The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term for the Company's stock options was calculated based on the weighted-average vesting term of the awards and the contract period, or simplified method.
- *Expected volatility*—Since the Company is not yet a public company and does not have any trading history for its common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their size, stage in the life cycle or area of specialty. The Company will continue to apply this process until enough historical information regarding the volatility of its stock price becomes available.
- *Risk-free interest rate*—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.
- *Expected dividend*—The Company has never paid dividends on the common stock and has no plans to pay dividends on the common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of the common stock has been determined using independent third-party valuations based on relevant valuation methodologies as outlined in the American Institute of Certified Public Accountants (AICPA) Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. The Company also considered the amount of time between the independent third-party valuation dates and the grant dates and performed an interpolation of the fair value between the two valuation dates to estimate common stock fair value at each grant date. This determination included an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

Comprehensive Loss

Comprehensive loss includes all changes in equity (net assets) during a periodfrom non-owner sources. There have been no items qualifying as other comprehensive income or loss, and as such, comprehensive loss was the same as net loss for the periods presented.

Foreign Currency Transactions

Transactions denominated in foreign currencies are initially measured in U.S. dollars using the exchange rate on the date of the transaction. Foreign currency denominated monetary assets and liabilities are

subsequently re-measured at the end of each reporting period using the exchange rate at that date, with the corresponding foreign currency transaction gain or loss recorded in the statements of operations and comprehensive loss and statements of cash flows. Nonmonetary assets and liabilities are not subsequently re-measured.

Net Loss Per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, redeemable convertible preferred stock, common stock subject to repurchase, restricted common shares issued, and stock options are considered to be potentially dilutive securities.

Basic and diluted net loss attributable to common stockholders per share is presented in conformity withthe two-class method required for participating securities. The Company's redeemable convertible preferred stock contains participation rights in any dividend paid by the Company and is deemed to be a participating security. Restricted shares issued to the founders and upon early exercise of stock options also participate in dividends from the issuance date and are considered participating securities. Participating securities do not have a contractual obligation to share in losses. As such, the net loss was attributed entirely to common stockholders. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

Adopted and Recent Accounting Pronouncements

The Company is a smaller reporting company and an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay the adoption of new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. Thus, the Company has elected to use the extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that (i) the Company is no longer an emerging growth company or (ii) the Company affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. However as described below, the Company early adopted certain accounting standards, as the JOBS Act does not preclude an emerging growth company from adopting a new or revised accounting standard earlier than the time that such standard applies to private companies to the extent early adoption is permitted.

Recently Adopted Accounting Pronouncements

Effective January 1, 2019, the Company adopted Accounting Standard Update ("ASU") 2016-09, *Improvements to Employee Share Based Payment Accounting*. This ASU affects entities that issue share-based payment awards to their employees. The ASU is designed to simplify several aspects of accounting for share-based payment award transactions which include—the income tax consequences, classification of awards as either equity or liabilities, classification on the statement of cash flows and forfeiture rate calculations. As the Company did not have any significant stock-based compensation at the time of adoption, the adoption did not have a material impact on its financial statements.

Effective January 1, 2019, the Company adopted ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606*. The ASU clarifies certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement

participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. As the Company did not have any collaborative arrangements at the time of adoption, the adoption had no impact on its financial statements.

Effective January 1, 2019, the Company adopted ASU 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*. Prior to the adoption of ASU 2018-07, the measurement date for non-employee awards was generally the date the services are completed, resulting in financial reporting period adjustments to share-based compensation during the vesting terms for changes in the fair value of the awards. After the adoption of ASU 2018-07, the measurement date for non-employee awards is the date of grant without changes in the fair value of the award. The adoption had no impact on the Company's financial statements.

Effective January 1, 2019, the Company adopted ASU No. 2018-13, *Fair Value Measurement (Topic 820), Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. This ASU removed the following disclosure requirements: (i) the amount of and reasons for transfers between Level I and Level 2 of the fair value hierarchy; (ii) the policy for timing of transfers between levels; and (iii) the valuation processes for Level 3 fair value measurements. Additionally, this update added the following disclosure requirements: (1) the changes in unrealized gains and losses for the period included in other comprehensive income and loss for recurring Level 3 fair value measurements held at the end of the reporting period; and (2) the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements. For certain unobservable inputs, an entity may disclose other quantitative information (such as the median or arithmetic average) in lieu of the weighted average if the entity determines that other quantitative information would be a more reasonable and rational method to reflect the distribution of unobservable inputs used to develop Level 3 fair value measurements. ASU No. 2018-13 is effective for fiscal years beginning after December 15, 2019 with early adoption permitted. The adoption of ASU 2018-13 had no material impact on the Company's financial statements.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board ("FASB") issued ASU No. 2016-02, *Leases ("Topic 842")*. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases today. For non-public entities, ASU 2016-02 is effective for annual reporting periods beginning after December 15, 2020, including interim periods within those fiscal years, and early adoption is permitted. The Company plans to adopt the new standard as of January 1, 2021 on a modified retrospective basis. At adoption, the Company has one lease with the remining term of less than 12 months and, as such, it will not record any cumulative adjustment on its balance sheet. In the first quarter of 2021, the Company entered in a long-term lease, for which it will record the related right-of-use asset and lease liability (Note 12).

In June 2016, the FASB issued ASU 2016-13, *Credit Losses*. The FASB also issued amendments and the initial ASU, and all updates are included herein as the Credit Losses standard or Topic 326. The new standard generally applies to financial assets and requires those assets to be reported at the amount expected to be realized. The ASU is effective for fiscal years beginning after December 15, 2021 and interim periods within those fiscal years. The Company is currently evaluating the potential impact of this standard on its financial statements.

Graphite Bio, Inc.
Notes to Financial Statements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740)*. The amendments in ASU 2019-12 simplify the accounting for income taxes by removing certain exceptions to the general principles in Topic 740. The amendments also improve consistent application of and simplify U.S. GAAP or other areas of Topic 740 by clarifying and amending existing guidance. The new standard is effective for the Company on January 1, 2022 and for interim periods beginning on January 1, 2023. The Company is currently evaluating the potential impact of this standard on its financial statements.

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* (ASU 2020-06), which simplifies the accounting for convertible instruments by reducing the number of accounting models available for convertible debt instruments. This guidance also eliminates the treasury stock method to calculate diluted earnings per share for convertible instruments and requires the use of the if-converted method. This guidance will be effective for the Company in the first quarter of 2022 on a full or modified retrospective basis, with early adoption permitted. The Company is currently evaluating the potential impact of this standard on its financial statements.

3. Fair Value Measurements

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets, as well as assets and liabilities measured at fair value on a non-recurring basis or disclosed at fair value, are categorized based upon the level of judgment associated with inputs used to measure their fair values. The accounting guidance for fair value provides a framework for measuring fair value and requires certain disclosures about how fair value is determined. Fair value is defined as the price that would be received upon the sale of an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance also establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1 — Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 — Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3 — Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. An assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. Changes in the ability to observe valuation inputs may result in a reclassification of levels of certain securities within the fair value hierarchy. The Company recognizes transfers into and out of levels within the fair value hierarchy in the period in which the actual event or change in circumstances that caused the transfer occurs.

Graphite Bio, Inc.
Notes to Financial Statements

As of December 31, 2019, the Company did not have any financial instruments measured at fair value on a recurring basis. As of December 31, 2020, Level 1 securities consist of highly liquid money market funds for which the carrying amounts approximate their fair values due to their short maturities. Level 3 liabilities that are measured at fair value on a recurring basis include the redeemable convertible preferred stock tranche liability. The redeemable convertible preferred stock tranche liability is measured using the option pricing method by estimating the value using the Black-Scholes model. The inputs used in the Black-Scholes model includes the fair value of the redeemable convertible preferred stock, the risk-free interest rate, the expected volatility and the expected term when each tranche will be settled.

Below are inputs used for the Level 3 liabilities in the year ended December 31, 2020:

	Redeemable Convertible Preferred Stock Tranches Liability	
	As of Issuance June 24, 2020	As of December 31, 2020(1)
Value of Series A Preferred Stock per share	$ 0.78	$ 2.94
Risk-free rate	0.16% - 0.18%	0.08%
Expected volatility	66.3%	85.7%
Term (in years)	0.50 - 1.08	0.13

(1) Includes assumptions for the tranche settled on December 28, 2020.

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the year ended December 31, 2020.

The following tables set forth the financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy at December 31, 2020 (in thousands):

	December 31, 2020			
	Total Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds(1)	$ 19,782	$19,782	$ —	$ —
Liabilities:				
Redeemable convertible preferred stock tranche liability	$ 29,062	$ —	$ —	$29,062

(1) Included within cash and cash equivalents on the balance sheet.

The following table provides a summary of changes in the estimated fair value of Level 3 financial instruments (in thousands):

	Redeemable Convertible Preferred Stock Tranche Liability
Balance as of December 31, 2019	$ —
Fair value of Series A redeemable convertible preferred stock tranche liabilities issued in 2020	3,329
Change in fair value	54,833
Settlement of Series A redeemable convertible preferred stock tranche liability	(29,100)
Balance as of December 31, 2020	$ 29,062

4. Balance Sheet Components

Property and Equipment, Net

As of December 31, 2019, the Company did not have any property and equipment. Property and equipment, net as of December 31, 2020, consists of the following (in thousands):

Computers and network equipment	$ 24
Lab equipment	1,558
Less: accumulated depreciation	(121)
Total property and equipment, net	$1,461

Depreciation expense for the year ended December 31, 2020 was $121,000.

5. Accrued Expenses

Accrued expenses as of December 31, 2019 and 2020, consisted of the following (in thousands):

	December 31,	
	2019	2020
Preclinical studies	$ —	$1,764
Professional fees	19	55
Other accrued expenses	—	71
Total accrued expenses	$ 19	$1,890

6. Significant Agreements

Stanford Exclusive License Agreement

In December 2020, we entered into an exclusive license agreement (the License Agreement), with The Board of Trustees of the Leland Stanford Junior University (Stanford), pursuant to which Stanford granted us a worldwide license to specified technology and patent rights to develop, manufacture and commercialize human prophylactic and therapeutic products. Other than with respect to specified, broadly applicable assays and procedures and subject to retained rights by Stanford, the license is exclusive with respect to human prophylactic

and therapeutic products for the treatment of SCD, XSCID and beta thalassemia. The license is non-exclusive with respect to those broadly applicable assays and procedures and with respect to all human prophylactic and therapeutic products other than for the treatment of SCD, XSCID and beta thalassemia.

Pursuant to the License Agreement, we paid an upfront license fee of $50,000, and as additional consideration for the license, we agreed to issue to Stanford approximately 1,558,587 shares of our common stock. As of December 31, 2020, the Company recorded its obligations to issue Stanford shares of common stock at an estimated fair value of $2.8 million to additional paid in capital. The common shares are expected to be issued when Stanford provides the inventors' names for allocation of the shares. Stanford also had an option to buy up to 10% of newly issued shares in the future private financings at the price paid by other participating investors.

The acquisition of the exclusive license, including patent rights andknow-how, and clinical supplies was accounted for as an asset acquisition and as the acquired technology and inventories did not have an alternative use, the total consideration of $2.8 million was recorded as research and development expense in the statements of operations and comprehensive loss for the year ended December 31, 2020.

In connection with the License Agreement, the Company reimbursed Stanford $177,947 for previously incurred patent costs, which were recorded in general and administrative expenses for the year ended December 31, 2020 and, in addition, is obligated to reimburse future patent costs. The Company is also obligated to pay annual maintenance fees as follows: $5,000 in the first year, $10,000 in each year 2 and 3, $25,000 in each year 3 through 6, $50,000 each subsequent year until first commercial sale and $200,000 each subsequent year after the first commercial sale.

The Company is also obligated to make future development and regulatory milestones in total of up to $5.3 million, sales based milestones of up to $7.5 million and royalties on future sales at percentage rates ranging in the low single digits. In addition, if the Company receives any sublicense income, it is required to share it with Stanford as a certain percentage defined for each milestone in the License Agreement. The Company will record the maintenance fees, when payable, and will record milestones when contingencies are resolved, and milestones are due. No milestones were achieved and recorded as of December 31, 2020.

The term of the License Agreement expires on the later of (a) the expiration of the last patent or abandonment of the last patent application within the license patent rights or (b) the expiration of all royalty terms with respect to Licensed Products.

The Stanford License terminates on a product by product and country by country basis on the latest to occur of (i) expiration of the last valid claim of a licensed patent that covers the sale or manufacture of the applicable licensed product in such country, (ii) expiration of any period of regulatory exclusivity granted with respect to such licensed product in such country or (iii) ten years after the first commercial sale of such licensed product in a country Stanford also has a right to terminate the agreement if milestones plan is rejected by Stanford as specified in the License Agreement.

7. Commitments and Contingencies

Research and Development Agreements

The Company enters into contracts in the normal course of business with CROs for clinical trials, with contract manufacturing organizations for CMOs with other vendors for preclinical studies, supplies and other services and products for operating purposes. These contracts generally provide for termination on notice or may have a potential termination fee if a purchase order is cancelled within a specified time. As of December 31, 2019, and 2020, there were no amounts accrued related to termination and cancellation charges as the Company has not determined cancellation to be probable.

Graphite Bio, Inc.
Notes to Financial Statements

License Agreements

The Company entered into the License Agreement (Note 6), pursuant to which the Company is required to pay certain cash milestones contingent upon the achievement of specific events. No such milestones were achieved or probable as of December 31, 2020. The Company is required to pay royalties on sales of products developed under this agreement. All products are in development as of December 31, 2020 and no such royalties were due.

Legal Contingencies

From time to time, the Company may become involved in legal proceedings arising from the ordinary course of business. The Company records a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. Management is currently not aware of any legal matters that could have a material adverse effect on financial position, results of operations or cash flows.

Operating Leases

In May 2020, the Company entered into a one-year lease agreement for its headquarter facility located in South San Francisco, California with a significant portion of premises allocated to research lab. Due to COVID-19, the use of the entire facility was designated to research and, as such, all associated costs were expensed as research and development. In addition to payment of base rent, the Company is also required to pay property taxes, insurance and common area expenses. The Company records rent expense on a straight-line basis over the term of the lease. The term of the lease is from May 8, 2020 to June 30, 2021, with an option to renew.

As of December 31, 2020, the Company had a remaining obligation for the base rent in the amount $0.2 million.

Guarantees and Indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. Its exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To the extent permitted under Delaware law, the Company has agreed to indemnify its directors and officers for certain events or occurrences while the director or officer is, or was serving, at a request in such capacity. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2019, and 2020, the Company did not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

8. Redeemable Convertible Preferred Stock

Series A Redeemable Convertible Preferred Stock

In June 2020, the Company issued 10,000,000 shares of its Series A redeemable convertible preferred stock at a price of $1.00 per share for gross cash proceeds of $10.0 million and issued 5,019,949 shares of its Series A redeemable convertible preferred stock upon the conversion of the outstanding convertible note and accrued interest.

Graphite Bio, Inc.
Notes to Financial Statements

In connection with the initial issuance of the shares of its Series A redeemable convertible preferred stock, the Company had an obligation to sell and the holders had the obligation to purchase the additional 30,000,000 shares of Series A redeemable convertible preferred stock at $1.00 per share upon the achievement of certain milestones as determined by the Board and approved by at least one of the investors, or upon the waiver of such milestones by the holders of at least 75% of the outstanding shares of Series A redeemable convertible preferred stock, in two equal tranches of $15.0 million each. The Company determined that the obligation to sell additional shares is a freestanding financing instrument and a liability. The Company estimated the fair value of the liability to be $3.3 million and recorded it as a reduction to redeemable convertible preferred stock and as a derivative redeemable convertible preferred stock tranche liability in its balance sheet at the issuance date.

In December 2020, the requisite holders waived the second tranche milestone event and the Company issued 15,000,000 shares of its Series A redeemable convertible preferred stock for gross cash proceeds of $15.0 million. The redeemable convertible preferred stock tranche liability related to the second tranche shares was remeasured to fair value of $29.1 million and reclassified to redeemable convertible preferred shares upon the settlement.

In connection with the issuance of Series A redeemable convertible preferred stock, in the year ended December, 31, 2020, the Company incurred issuance costs of $184,000.

As of December 31, 2020, the redeemable convertible preferred stock tranche liability related to the third tranche shares was remeasured at fair value of $29.1 million and continued to be reported in current liabilities. The Company settled the third tranche in February 2021, prior to the closing of the Series B financing (refer to Note 14) and issued 15,000,000 shares of its Series A redeemable convertible preferred stock for gross cash proceeds of $15.0 million. The Company recognized a total of $54.8 million as other loss in the statements of operations and comprehensive loss related to the changes in the fair value of the redeemable convertible preferred stock tranche liabilities during the year ended December 31, 2020.

As of December 31, 2020, the Company was authorized to issue 45,024,986 shares and had issued 30,019,945 shares of its Series A redeemable convertible preferred stock with the following rights, preferences and privileges:

Dividends—The holders of Series A redeemable convertible preferred stock are entitled to receive noncumulative dividends at the rate of 8% per share of the original issuance price, when, as and if declared by the Board. No dividends or other distributions shall be made with respect to the common stock unless dividends on the preferred stock have been declared in accordance with the preferences stated within the certificate of incorporation and all declared dividends on the preferred stock have been paid. No dividends were declared and paid or payable in the year ended December 31, 2020.

Liquidation Rights—In the event of the liquidation, dissolution, or winding up of the Company, or a deemed liquidation event, including a merger or consolidation, or a sale or other disposition of all or substantially all of the Company's assets, the holders of shares of Series A preferred stock are entitled to receive, before any payment are made to the holders of common stock, an amount per share equal to the greater of (i) the Series A original issue price $1.00, plus any dividends declared but unpaid, or (ii) such amount per share as would have been payable had all shares of Series A preferred stock been converted into common stock immediately prior to such liquidation, dissolution, winding up or deemed liquidation. The remaining assets of the Company available for distribution to its stockholders will be distributed (1) first, pro rata among the holders of the common stock and Series A preferred stock on an as-converted basis, until the holders of the Series A preferred stock have received an aggregate of three times the original purchase price per share plus all declared and unpaid dividends on such shares and (2) second, among the holders of shares of common stock, pro rata based on the number of shares held by each such holder.

Graphite Bio, Inc.
Notes to Financial Statements

***Conversion*—**Each share of Series A preferred stock is be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder, into such number of shares of common stock as is determined by dividing the Series A original issue price ($1.00) by the Series A conversion price in effect at the time of conversion. The Series A conversion price is initially equal to the Series A original issue price. Such initial Series A conversion price, and the rate at which shares of Series A preferred stock may be converted into shares of common stock, is subject to recapitalization and other adjustments as provided in the certificate of incorporation. In the event of a liquidation, dissolution or winding up of the Company or a deemed liquidation event, the conversion rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Series A preferred stock.

All outstanding shares of Series A preferred stock are automatically converted into shares of common stock, at the then effective Series A conversion price and such shares may not be reissued by the Company upon either: (i) the closing of the sale of shares of common stock to the public at a price per share of at least three times the Series A original issue price, in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $50.0 million of gross proceeds to the Company (before deduction of estimated underwriting discounts and commissions and offering expenses payable by the Company) and in connection with such offering the common stock is listed for trading on the Nasdaq Stock Market's Global Market, the New York Stock Exchange or another exchange or marketplace approved by the Board (including in any event, at least one of the preferred directors), or (ii) upon a receipt of a written request for such conversion from the holders of at least 75% of the redeemable convertible preferred stock then outstanding.

In addition, if any holder of shares of Series A preferred stock fails to purchase all of the shares required to be purchased by such holder at a tranche milestone closing and becomes a defaulting purchaser, then each share of Series A preferred stock held by such holder immediately prior to the tranche milestone closing will automatically and without any further action on the part of the Company or such holder, be converted into fully-paid and non-assessable shares of common stock at the rate of 10 shares of Series A preferred stock to one share of common stock. In addition, any common shares owned by such holder at the time of default would also convert at the ratio of 10 shares of common stock to one share of common stock. All investors participated in the second tranche closing and special mandatory conversion was not triggered.

Voting Rights—Except for certain matters or as required by law, the holders of redeemable convertible preferred stock and the holders of common stock vote together and not as separate classes. Each holder of Series A preferred stock is entitled to the number of votes equal to the number of shares of common stock into which the shares of Series A preferred stock could be converted as of the record date.

Certain protective provisions, such as any actions that could adversely affect the Series A preferred stock rights and privileges, alter the capital structure, increase or decrease the size of the Board, or effect any liquidation event, require approval of at least 75% of the outstanding shares of redeemable convertible preferred stock, voting as a single class on an as-converted basis.

Series A redeemable convertible preferred stockholders, voting as a separate class, are entitled to elect three members of the Board (the "preferred directors"). Common stockholders, voting as a separate class, are entitled to elect two members of the Board. The remaining members of the Board are elected by the holders of redeemable convertible preferred stock and common stock, voting together as a single class on an as-converted basis.

Graphite Bio, Inc.
Notes to Financial Statements

Redemption—Upon the occurrence of certain change in control events that are outside of the Company's control, including liquidation, sale or transfer, holders of the redeemable convertible preferred stock can effectively cause redemption for cash. As a result, the Company classified the redeemable convertible preferred stock as mezzanine equity on the balance sheets as the stock is contingently redeemable.

9. Common Stock

Immediately prior to the effectiveness of domestication and incorporation in the State of Delaware, as described in the Note 1, the Company's outstanding capital consisted of one share with par value of $0.0001 (the "Canadian Share"). Upon effectiveness of the domestication in October 2019, one Canadian Share outstanding converted into one share of common stock with par value of $0.001, which was outstanding at December 31, 2019.

As of December 31, 2020, the Company was authorized to issue 80,000,000 shares of its common stock with $0.00001 par value per share. As of December 31, 2020, 24,998,807 shares of common stock were issued and outstanding. Each share of the Company's common stock is entitled to one vote.

Shares Reserved for Future Issuance

As of December 31, 2020, the Company reserved common stock for future issuances as follows:

Redeemable convertible preferred stock	30,019,945
Outstanding stock option awards	746,000
Shares available for future stock option grants	5,020,152
Total shares reserved for future issuance	35,786,097

Founders' and Investor's Restricted Common Stock

In March 2020 the Board approved and in April 2020, the Company issued 14,790,000 shares of its common stock to its founders and 5,999,999 shares of its common stock to its investor at the purchase price of $0.00001 per share. As of December 31, 2020, the investor's shares were fully vested and a portion of the shares issued were subject to the Company's option to repurchase per the Stanford Adjustment Repurchase Right, as described below.

The shares of the Company's common stock issued to its founders for their advisory and consulting services vest monthly over four years with one year cliff from the vesting commencement date. The vesting commencement date was the date of the initial closing of the Series A preferred stock financing or June 24, 2020. Per the Series A agreement, the vesting of the founders' common stock shares could be accelerated upon signing of term-sheet for the license with Stanford, a change in control, or if the service is terminated by the Company without cause. The Company signed the term sheet with Stanford in June 2020 and as a result 2,218,500 shares of founders' common stock vested pursuant to the acceleration terms.

If a founder terminates the relationship with the Company during the vesting period, the Company may repurchase any unvested restricted common stock at the price per share equal to the lower of (i) the original purchase price, subject to adjustment in the event of any reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or (ii) the current fair market value as of the date the Company elects to exercise this repurchase. The repurchase right lapses in 180 days after the termination of the founder's service or employment. During the vesting term, holders of founders' common stock awards are deemed to be common stockholders and have the right to receive dividends and voting rights.

The founders' shares of common stock are also subject to the Company's option to repurchase per the Stanford Adjustment Repurchase Right, as described below.

The Company accounts for shares issued to founders as equity compensation awards and the estimated fair value at the grant date was minimal. As of December 31, 2020, 12,571,500 shares of founders' common stock awards were unvested and expected to vest in 3.5 years.

Stanford Adjustment Repurchase Right: upon the issuance of shares of common stock to Stanford pursuant to the License Agreement, as discussed in Note 6, the Company has a right to repurchase from each founder and an investor a number of shares of common stock equal to the number of shares issued to Stanford multiplied the applicable number of shares issued to the founder or investor, as applicable, divided by 17,690,000 shares (a fully diluted number of shares of the Company at the end of March 2020, after founders and the investor's shares were approved by the board of directors). The Stanford Adjustment Repurchase Right may be exercised by the Company within six months following the date of the issuance of the shares of common stock to Stanford. The repurchase price per share is equal to the lower of (i) the purchase price, subject to adjustment in the event of any reorganization, recapitalization, reclassification, etc., or (ii) the current fair market value as of the date the Company elects to exercise its Stanford Adjustment Repurchase Right. As of December 31, 2020, the Company did not issue any shares of common stock to Stanford and did not repurchase any founders' or the investor's shares. The Company accounts for founders and investor's shares of restricted common stock as equity share-based awards.

10. Equity Incentive Plans

The Company grants share-based awards under the 2020 Stock Option Plan, as amended (the "2020 Plan"). The Company may grant under the 2020 Plan incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units and other share-based awards to the Company's officers, employees, directors and consultants. Options under the 2020 Plan may be granted for periods of up to 10 years and at prices no less than 100.0% of the estimated fair value of the shares on the date of grant as determined by the Board, provided, however, that the exercise price of an incentive stock option granted to a 10.0% stockholder shall not be less than 110.0% of the estimated fair value of the shares on the date of grant and the option is not exercisable after the expiration of five years from the date of grant. Options generally vest monthly over four years with or without one year cliff vesting. Per the 2020 Plan, granted options maybe early exercised and the Company will issue shares of restricted stock upon the early exercise with vesting terms consistent with the original grant.

As of December 31, 2020, 9,974,959 shares were reserved for issuance under the 2020 Plan and 5,020,152 shares were available for future grants. The table below presents a summary of activities and a reconciliation of common shares remaining for grant under the 2020 Plan:

Shares authorized under 2020 Plan	9,974,959
Options granted	(2,928,986)
Restricted stock awards granted	(2,025,821)
Remaining shares available for grant as of December 31, 2020	5,020,152

Restricted Stock Awards

The Company issued 2,025,821 shares as restricted stock awards under the 2020 Plan. The purchase price of the restricted common stock awards was fair value as determined by the Board at the issuance date. The shares vest monthly over four years with the one-year cliff vesting from the grant date. Upon termination of employment, the Company has the right to repurchase any unvested restricted shares. The repurchase price for unvested shares of common stock will be the lower of (i) the fair market value on the date of repurchase or (ii) their original purchase price.

Graphite Bio, Inc.
Notes to Financial Statements

The Company accounted for restricted stock awards as early exercised options and recognized a liability in other liabilities when cash was received for the purchase of shares of restricted stock awards. As shares of restricted stock awards vest, the Company reclassified the liability to common stock and additional paid in capital. As of December 31, 2020, the Company recorded a liability for restricted stock awards included in other liabilities of $36.

The Company used the Black-Scholes option pricing model to estimate stock-based compensation expense related for issued restricted stock awards with the following assumptions for the year ended December 31, 2020:

Expected volatility	66.30% - 67.60%
Expected dividend yield	0%
Expected term (in years)	2.84 - 3.12
Risk-free interest rate	0.16% - 0.39%

Awards granted during the year ended December 31, 2020 had an estimated weighted average grant date fair value per share of $0.02 and the total fair value of such awards was $36,000. No restricted stock awards shares were cancelled, repurchased or vested as of December 31, 2020. Total intrinsic value of outstanding unvested restricted stock awards was $4.0 million as of December 31, 2020. There was no activity for restricted stock awards in the year ended December 31, 2019.

Incentive Stock Options and Nonqualified Stock Options

Stock options issued under the 2020 Plan, generally, vest over a four-year period and expire ten years from the date of grant. Certain options provide for accelerated vesting if there is a change in control, as defined in the individual award agreements.

The Company used the Black-Scholes option pricing model to estimate stock-based compensation expense for stock option awards with the following assumptions for the year ended December 31, 2020:

Expected volatility	77.91% - 79.18%
Expected dividend yield	0%
Expected term (in years)	5.91 - 6.07
Risk-free interest rate	0.37% - 0.53%

A summary of option activity under the 2020 Plan is as follows:

	Number of Options	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	—	$ —	—	—
Granted	2,928,986	$ 0.12		
Exercised	(2,182,986)	$ 0.12		
Outstanding as of December 31, 2020	746,000	$ 0.12	9.9	$ 1,365
Exercisable	—	$ —	—	$ —
Vested and expected to vest at December 31, 2020	746,000	$ 0.12	9.9	$ 1,365

Graphite Bio, Inc.
Notes to Financial Statements

Aggregate intrinsic value represents the difference between the fair value of the underlying common stock and the exercise price as of December 31, 2020. The weighted-average grant date fair value of options granted in 2020 is $1.04. The intrinsic value of the stock options exercised was $2.8 million for the year ended December 31, 2020. There was no activity for options in the year ended December 31, 2019.

Early Exercise of Stock Options

The terms of the 2020 Plan permit the exercise of options granted prior to vesting, subject to required approvals. The unvested shares are subject to the repurchase right upon termination of employment at the original purchase price. The repurchase right lapses in 180 days after the termination of the employee's employment. Shares purchased by employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be issued until those shares vest according to their respective vesting schedules. Cash received for early exercised stock options is recorded as other liabilities on the balance sheet and is reclassified to common stock and additional paid-in capital as such shares vest.

At December 31, 2020, 2,103,994 shares remained subject to the right of repurchase as a result of the early exercised stock options. The remaining liability related to early exercised shares as of December 31, 2020 was $0.3 million and was recorded in other liabilities in the balance sheet.

Stock-Based Compensation Expense

The following table presents the components of stock-based compensation expense for the Company's stock-based awards for the year ended December 31, 2020 (in thousands):

Restricted stock awards and founders' common stock awards	$ 6
Stock options	171
Total stock-based compensation expense	$177

The following table presents the classification of stock-based compensation expense for the Company's stock-based awards for the year ended December 31, 2020 (in thousands):

Research and development expenses	$123
General and administrative expenses	54
Total stock-based compensation expense	$177

As of December 31, 2020, there was $2.9 million of unrecognized stock-based compensation expense related to the employee andnon-employee awards, which is expected to be recognized over a weighted-average period of 3.7 years. There was no stock-based compensation expense recognized in the year ended December 31, 2019.

Graphite Bio, Inc.
Notes to Financial Statements

11. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of basic and diluted net loss per share in the year ended December 31, 2020 attributable to common stockholders, which excludes shares which are legally outstanding, but subject to repurchase by the Company (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2019	2020
Numerator:		
Net loss	$ (109)	$ (68,373)
Denominator:		
Weighted-average common shares outstanding	1	17,033,101
Less: Weighted-average unvested restricted shares and shares subject to repurchase	—	(11,478,202)
Weighted-average shares used to computing basic and diluted net loss per share	1	5,554,899
Net loss per share attributable to common stockholders—basic and diluted:	($109,000.00)	($ 12.31)
Anti-dilutive outstanding shares or equivalents		
Redeemable convertible preferred stock	—	30,019,945
Options to purchase common stock	—	746,000
Unvested restricted common stock	—	14,597,321
Total	—	45,363,266

As of December 31, 2019, 1 common share was issued and outstanding and total net loss of $109,000 was allocated to this share. No other securities were outstanding as of December 31, 2019 that potentially might be dilutive.

12. Related Party Transactions

Related Party Convertible Notes and Expenses Reimbursement

In June 2017, the Company issued a convertible promissory note (the "2017 Note") to its sole investor, Versant, for $2.0 million with 4% annual interest rate payable upon maturity in December 2018. The outstanding principal amount of the 2017 Note and any unpaid accrued interest were automatically convertible into preferred shares sold in a qualified financing, as defined in the agreement at a conversion price equal to the lesser of: 80% the purchase price paid per preferred share, and $5.0 million divided by the aggregate number of the Company's fully diluted equity immediately prior to the closing of the qualified financing. The Company could not prepay the 2017 Note without the consent of the holder. In an event of change of control, the holder could, at the option of the holder and upon written notice to the Company, elect to convert the principal and accrued interest as of the date of such election (if not previously converted or repaid) into number of shares of the Company's common shares at the conversion price equal to $3.0 million divided by the aggregate number of the Company's fully diluted equity immediately prior to the date of such election. On the maturity date, the holder could, at the option of the holder and upon a written notice to the Company, elect to convert the principal and accrued interest into number of shares of a newly designated series of the Company's preferred shares (at the conversion price equal to $3.0 million divided by the aggregate number of the Company's fully diluted equity prior to the maturity date. Upon an event of default, as defined in the agreement, at the option and upon the declaration of the holder and upon written notice to the Company, all principal and unpaid accrued interest would become due and payable.

As of December 31, 2019, the 2017 Note was outstanding and in default and continued to accrue interest at 4% per year. In April 2020, the outstanding principal and accrued interest of $2.3 million was forgiven and the transaction was recorded to additional paid in capital as a related party investor note forgiveness. The Company accounted for the forgiveness as a debt extinguishment. The estimated fair values of the embedded share-settlement put option and default options were minimal as of December 31, 2019 and as of the cancellation date.

In March 2020, the Company issued a new convertible promissory note (the 2020 Note) for $5.0 million to the same investor with an interest rate of 1.6% per annum payable at maturity in March 2021. The outstanding principal amount of the 2020 Note and any unpaid accrued interest were automatically convertible into the Company's preferred shares sold in a qualified financing, as defined in the agreement, into that number of preferred shares sold in such qualified financing as is equal to the quotient of (i) the conversion amount (note principal and accrued interest) divided by (ii) the per share price at which the preferred shares are sold in such qualified financing and on such other terms and conditions provided to investors in the qualified financing. The Company could not prepay the note without the consent of the holder. In an event of change of control, the holder could, at the option of the holder and upon written notice to the Company, elect to convert the principal and accrued interest as of the date of such election (if not previously converted or repaid) into number of shares of the Company's common shares at the conversion price equal to $31.7 million divided by the aggregate number of the Company's fully diluted equity immediately prior to the date of such election. On the maturity date, the holder could, at the option of the holder and upon a written notice to the Company, elect to convert the principal and accrued interest into number of shares of a newly designated series of the Company's preferred shares (at the conversion price equal to $31.7 million divided by the aggregate number of the Company's fully diluted equity prior to the maturity date. Upon an event of default, as defined in the agreement, at the option and upon the declaration of the holder and upon written notice to the Company, all principal and unpaid accrued interest would become due and payable.

The principal and accrued interest of the 2020 Note were converted to 5,019,945 shares of the Company's Series A redeemable convertible preferred stock in June 2020, per its embedded share-settlement put option provision. Issued preferred shares were recorded at fair value at the issuance date, and there was no extinguishment gain or loss recorded on the conversion.

During 2020, the Company reimbursed certain expenses to the same investor, primarily due diligence, legal and marketing expenses. As of December 31, 2020, the Company had recorded $86,000 in accrued expenses payable, of which $66,000 were recorded as preferred stock financing issuance costs and $20,000 as general and administrative expenses.

Founders Consulting Agreements and Expenses Reimbursement

In March 2020, the Company entered into the consulting agreements with two founders, who also received founders' common stock shares. The Company paid $107,000 for board services, advisory and consulting services, which were recorded as general and administrative expenses in the statements of operations and comprehensive loss.

The Company also agreed to reimburse $250,000 of legal, travel and other expenses incurred by the founders prior to joining the Company, which were paid in September 2020. Founders' expenses are recorded as general and administrative expenses in the statements of operations and comprehensive loss.

13. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2019 and 2020. The Company has incurred net operating losses only in the United States since its inception. The Company has not reflected any benefit of such net operating loss carryforwards in the financial statements.

Graphite Bio, Inc.
Notes to Financial Statements

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate was as follows:

	Year Ended December 31,	
	2019	2020
Income tax computed at federal statutory rate	21.00%	21.00%
State taxes, net of federal tax benefit	1.83	0.17
Preferred stock tranche liability	—	(16.84)
Cancellation of debt	—	(0.61)
General business credit—federal	—	(0.05)
Interest expense	(15.42)	(0.01)
Other permanent differences	—	(0.13)
Change in valuation allowance	(7.41)	(3.53)
Effective income tax rate	—%	—%

Net deferred tax assets and liabilities consisted of the following (in thousands):

	As of December 31,	
	2019	2020
Deferred tax assets		
Net operating losses	$ 8	$ 2,269
Research and development credits	—	81
Accrued expenses	—	105
Gross deferred tax assets	8	2,455
Valuation allowance	(8)	(2,414)
Total deferred tax assets	—	41
Deferred tax liabilities		
Other	—	(41)
Total deferred tax liabilities	—	(41)
Net deferred tax balance	$ —	$ —

Net operating losses and tax credit carryforwards were as follows as of December 31, 2020 (dollars in thousands):

		Expiration Year
Net operating losses, federal (starting from January 1, 2018)	$ 10,793	Does not expire
Net operating losses, federal (before January 1, 2018)	—	—
Net operating losses, state	29	2039
Tax credits, federal	—	—
Tax credits, state	147	Does not expire

Utilization of the net operating loss carryforwards and research credit carryforwards may be subject to an annual limitation due to the ownership percentage change limitations provided by the Internal Revenue Code, as amended, ("IRC"), and similar state provisions. Annual limitations may result in the expiration of the net operating losses and tax credit carryforwards before they are utilized. The Company did not perform an IRC Section 382 analysis and any previous ownership changes may result in a limitation that will reduce the total

amount of net operating loss and tax credit carryforwards disclosed that can be utilized. Subsequent ownership changes may affect the limitation in future years.

During the years ended December 31, 2019 and 2020, the Company recorded a 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. Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2019 and 2020 related primarily to the increases in net operating loss carryforwards and research and development tax credit carryforwards and were as follows (in thousands):

	Year Ended December 31,	
	2019	2020
Valuation allowance at the beginning of the year	$ —	$ 8
Increases recorded to income tax provision	8	2,406
Valuation allowance at the end of the year	$ 8	$2,414

The Company's U.S. federal and state income tax returns are generally subject to tax examinations for the tax years from inception through December 31, 2020. 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.

As of December 31, 2020, the Company had no unrecognized tax benefits. The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2019 and 2020, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease during the next 12 months.

14. Subsequent Events

The Company has reviewed and evaluated subsequent events as of December 31, 2020 through April 16, 2021, the date that the financial statements were available to be issued.

On January 22, 2021, the Company entered into the first exclusive option agreement with Stanford for additional technologies and will pay $10,000 upon exercise of the option. In addition, upon exercise of the option, the Company will issue Stanford 321,358 shares of common stock.

On January 27, 2021, the Company entered into a new lease agreement for lab space in South San Francisco, CA which will commence on October 1, 2021. The term of the lease is 42 months with a right to extend the term of for additional two years on the same terms and conditions.

On February 16, 2021, the Company issued 15,000,000 shares of Series A redeemable convertible preferred stock with the settlement of the tranche liability for $15.0 million gross cash proceeds.

On March 4, 2021, the Company amended the Stanford License to increase the number of shares to be issued to Stanford in connection with the closing of the second tranche of Series A preferred financing from 459,433 to 478,325, and extended by a month the time when the shares are expected to be issued. On April 7, 2021, the Company amended the Stanford License again and extended the time when the shares will be issued by another month to May 7, 2021.

Graphite Bio, Inc.
Notes to Financial Statements

On March 11, 2021, the Company authorized and issued 29,792,487 shares of Series B redeemable convertible stock at the purchase price of $5.06 per share for a total of $150.7 million in gross cash proceeds. In connection with entering into Series B agreement, the Company increased the number of authorized shares of common stock to 120,000,000.

On April 13, 2021, the Company entered into the second exclusive option agreement with Stanford for additional technologies. Pursuant to the second option agreement, the Company agreed to pay Stanford option fees in an aggregate amount of $30,000 over the term of the option.

Table of Contents

Shares

Common Stock

Prospectus

Morgan Stanley **BofA Securities** **Cowen** **SVB Leerink**

, 2021

Part II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses, other than estimated underwriting discounts and commissions, payable in connection with the registration of the common stock hereunder. All amounts are estimates except the SEC registration fee, the Financial Industry Regulatory Authority, Inc. (FINRA) filing fee and the Nasdaq Global Market listing fee.

	Amount Paid or to Be Paid
SEC registration fee	$ *
FINRA filing fee	*
Nasdaq Global Market listing fee	*
Printing and mailing	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous	*
Total	$ *

* To be completed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law (DGCL), authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws to be in effect immediately prior to the completion of this offering that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements will provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance provided by their affiliates or other third parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we will agree in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We will maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act of 1933, as amended (the Securities Act).

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriters against certain liabilities under the Securities Act and the Securities Exchange Act of 1934.

Item 15. Recent Sales of Unregistered Securities.

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(a) Issuances of Capital Stock

On October 30, 2019, we converted one share of our common stock outstanding at our Company originally incorporated in Ontario, Canada, to one share of the company reincorporated in the State of Delaware at a purchase price of $0.001 in connection with our reincorporation.

In April 2020, we sold an aggregate of 20,789,999 shares of our common stock at a purchase price of $0.00001 per share, for an aggregate purchase price of approximately $208.00.

On June 24, 2020, we sold an aggregate of 15,019,945 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

On December 28, 2020, we sold an additional 15,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

On February 16, 2021, we sold an additional 15,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of approximately $15.0 million.

On March 11, 2021, we sold an aggregate of 29,792,487 shares of our Series B redeemable convertible preferred stock at a purchase price of $5.06 per share, for an aggregate purchase price of approximately $150.7 million.

The offers and sales of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(b) Grants and Exercises of Stock Options and Restricted Stock

Since March 31, 2018, we granted stock options to purchase 9,956,030 shares of our common stock to our employees, directors and consultants at a weighted average exercise price of $1.20 per share under the 2020 Plan. We sold an aggregate of 4,417,586 shares of common stock to employees, directors and consultants for cash consideration in the aggregate amount of $530,110 pursuant to the exercise of stock options under the 2020 Plan.

The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under the registrant's 2020 Stock Plan. The shares of common stock issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial Statement Schedules.

None.

Exhibit Index

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1*	Amended and Restated Certificate of Incorporation, as amended, of the Registrant, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect immediately prior to completion of the offering.
3.3*	Bylaws of the Registrant and the amendments thereto, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon completion of the offering.
4.1*	Specimen Common Stock Certificate.
4.2*	Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders, dated March 11, 2021.
5.1*	Opinion of Goodwin Procter LLP.
10.1*#	2020 Stock Option and Grant Plan and forms of award agreements thereunder.
10.2*#	2021 Stock Option and Incentive Plan and forms of award agreements thereunder.
10.3*#	2021 Employee Stock Purchase Plan.
10.4*#	Senior Executive Cash Incentive Bonus Plan.
10.5*#	Non-Employee Director Compensation Policy.
10.6*#	Offer Letter, by and between the Registrant and Josh Lehrer, M.D., dated March 1, 2020.
10.7*#	Offer Letter, by and between the Registrant and Katherine V. Stultz, dated August 3, 2020.
10.8*#	Offer Letter, by and between the Registrant and Philip P. Gutry, dated September 15, 2020.
10.9*	Form of Indemnification Agreement by and between the Registrant and each of its directors and officers.
10.10*	Office Lease, by and between the Registrant and ARE-San Francisco No. 12, LLC, dated April 24, 2020, as amended by the First Amendment to Lease dated January 27, 2021.
10.11*	Laboratory Lease, by and between the Registrant and ARE-San Francisco No. 65, LLC, dated February 26, 2021.
10.12*†	Exclusive License Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated December 7, 2020.
10.13*†	Amendment No. 1 to the Exclusive License Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated March 4, 2021.
10.14*†	Amendment No. 2 to the Exclusive License Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated April 7, 2021.
10.15*†	Exclusive Option Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated January 22, 2021.
10.16*†	Exclusive Option Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated April 13, 2021.

Exhibit No.	Description
23.1*	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1).
24.1*	Power of Attorney (included on signature page).

* To be filed by amendment.
† Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit.
# Represents management compensation plan, contract or arrangement.

Signatures

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, California, on the day of , 2021.

GRAPHITE BIO, INC.

By: _____
Josh Lehrer, M.D.
Chief Executive Officer and Director

Power of Attorney

Each person whose individual signature appears below hereby authorizes and appoints Josh Lehrer, M.D. and Philip Gutry and each of them, with full power of substitution and resubstitution and full power to act without the other, as his true and lawful attorney in fact and agent to act in his name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Registration Statement, including any and all post effective amendments and amendments thereto, and any registration statement relating to the same offering as this Registration Statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys in fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys in fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated below.

Signature	Title	Date
Josh Lehrer, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	, 2021
Philip P. Gutry	Chief Business Officer, Head of Finance & Investor Relations (Principal Financial and Accounting Officer)	, 2021
Perry Karsen	Director	, 2021
Abraham Bassan	Director	, 2021
Jerel Davis, Ph.D.	Director	, 2021
Kristen M. Hege, M.D.	Director	, 2021

Table of Contents

Signature	Title	Date
Joseph Jimenez	Director	, 2021
Matthew Porteus, M.D., Ph.D.	Director	, 2021
Carlo Rizzuto, Ph.D.	Director	, 2021
Smital Shah	Director	, 2021
Jo Viney, Ph.D.	Director	, 2021