UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

Or

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

For the transition period from _____ to _____

Commission file number **001-15771**

ABEONA THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

Delaware	**83-0221517**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer I.D. No.)

1330 Avenue of the Americas, 33rd Floor, New York, NY 10019
(Address of principal executive offices, zip code)

(646) 813-4701
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Securities Exchange Act of 1934:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value	ABEO	Nasdaq Capital Markets

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

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

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

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

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

Large accelerated filer ☐
Non-accelerated filer ☒

Accelerated filer ☐
Smaller reporting company ☒
Emerging growth company ☐

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☐ No ☒

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the average bid and asked price of such common equity, as of June 30, 2020, was approximately $204,160,000.

The number of shares outstanding of the registrant's common stock as of March 19, 2021 was 98,788,933 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to our 2021 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year to which this

report relates.

TABLE OF CONTENTS

		Page
Part I		
Item 1.	Business	3
Item 1A.	Risk Factors	30
Item 1B.	Unresolved Staff Comments	65
Item 2.	Properties	65
Item 3.	Legal Proceedings	65
Item 4.	Mine Safety Disclosures	65
Part II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	66
Item 6.	Selected Financial Data	67
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	67
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	76
Item 8.	Financial Statements and Supplementary Data	76
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	77
Item 9A.	Controls and Procedures	77
Item 9B.	Other Information	77
Part III		
Item 10.	Directors, Executive Officers and Corporate Governance	78
Item 11.	Executive Compensation	78
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	78
Item 13.	Certain Relationships and Related Transactions, and Director Independence	78
Item 14.	Principal Accounting Fees and Services	78
Item 15.	Exhibits, Financial Statement Schedules	79
Item 16.	Form 10-K Summary	80
Signatures		81

FORWARD-LOOKING STATEMENTS

This Form 10-K (including information incorporated by reference) contains statements that express management's opinions, expectations, beliefs, plans, objectives, assumptions or projections regarding future events or future results and therefore are, or may be deemed to be, "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Words such as "expects," "anticipates," "intends," "plans," "believes," "could," "would," "seeks," "estimates," and variations of such words and similar expressions, and the negatives thereof, are intended to identify such forward-looking statements. We caution readers not to place undue reliance on any such "forward-looking statements," which speak only as of the date made, and advise readers that these forward-looking statements are not guarantees of future performance and involve certain risks, uncertainties, estimates, and assumptions by management that are difficult to predict. Various factors, some of which are beyond the Company's control, could cause actual results to differ materially from those expressed in, or implied by, such forward-looking statements. All such forward-looking statements, whether written or oral, and whether made by us or on our behalf, are expressly qualified by these cautionary statements and any other cautionary statements that may accompany the forward-looking statements. In addition, we disclaim any obligation to update any forward-looking statements to reflect events or circumstances after the date of this report, except as may otherwise be required by the federal securities laws.

Forward-looking statements necessarily involve risks and uncertainties, and our actual results could differ materially from those anticipated in forward-looking statements due to a number of factors. These statements include statements about: the potential impacts of the COVID-19 pandemic on our business, operations, and financial condition; the achievement of or expected timing, progress and results of clinical development, clinical trials and potential regulatory approvals; our Phase 3 clinical trial (VIITAL™) for patients with recessive dystrophic epidermolysis bullosa ("RDEB") and our beliefs relating thereto; our ability to identify and enroll patients in the Phase 3 clinical trial; our pipeline of product candidates; our use of the proceeds from the Paycheck Protection Program loan and our eligibility for loan forgiveness under the Coronavirus Aid, Relief and Economic Security Act, as amended; our belief that we have sufficient resources to fund operations for at least the next 12 months from the date of filing of this report; the ongoing arbitration proceeding with REGENXBIO; the dilutive effect that raising additional funds by selling additional equity securities would have on the relative equity ownership of our existing investors; our belief that EB-101 could potentially benefit patients with RDEB; our belief that adeno-associated virus ("AAV") gene therapy could potentially benefit patients with Sanfilippo syndrome type A ("MPS IIIA") and Sanfilippo syndrome type B ("MPS IIIB"); our ability to develop our novel AAV-based gene therapy platform technology; our belief in the adequacy of the data from clinical trials, including VIITAL™ and our Phase 1/2 clinical trials in ABO-102 (AAV-SGSH) for MPS IIIA and ABO-101 (AAV-NAGLU) for MPS IIIB, together with the data generated in the program to date, to support regulatory approvals; the existence of intellectual property, a license to which might be required to market MPS IIIA and MPS IIIB; our dependence upon our third-party and related-party customers and vendors and their compliance with regulatory bodies; our intellectual property position and our ability to obtain, maintain and enforce intellectual property protection and exclusivity for our proprietary assets; our estimates regarding the size of the potential markets for our product candidates, the strength of our commercialization strategies and our ability to serve and supply those markets; and future economic conditions or performance.

Important factors that could affect performance and cause results to differ materially from management's expectations are described in the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this Form 10-K. These factors include: the impact of the COVID-19 pandemic on our business, operations (including our clinical trials), and financial condition, and on our ability to access the capital markets; our ability to access our existing at-the-market sale agreement and any dilution that may result from accessing such sales agreement; our estimates regarding expenses, future revenues, capital requirements, and needs for additional financing; our ability to raise capital; our ability to fund our operating expenses and capital expenditure requirements for at least the next 12 months with our existing cash and cash equivalents; our ability to obtain additional equity funding from current or new stockholders, out-licensing technology and/or other assets, deferring and/or eliminating planned expenditures, restructuring operations and/or reducing headcount, and sales of assets; the dilutive effect that raising additional funds by selling additional equity securities would have on the relative equity ownership of our existing investors, including under our existing at-the-market sale agreement; our ability to continue to develop our novel AAV-based gene therapy platform technology; the outcome of any interactions with the U.S. Food and Drug Administration ("FDA") or other regulatory agencies relating to any of our products or product candidates; our ability to execute a Phase 3 clinical trial for patients with RDEB; our ability to complete enrollment of patients into clinical trials to secure sufficient data to assess efficacy and safety; our ability to identify additional patients for our Phase 1/2 clinical trial for patients with MPS IIIA and MPS IIIB; our ability to continue to secure and maintain regulatory designations for our product candidates; our ability to develop manufacturing capability compliant with current good manufacturing practices for our product candidates; our ability to manufacture gene and cell therapy products and produce an adequate product supply to support clinical trials and potentially future commercialization; the rate and degree of market acceptance of our product candidates for any indication once approved; and our ability to meet our obligations contained in license agreements to which we are party.

PART I

ITEM 1. BUSINESS

Business

Abeona Therapeutics Inc., a Delaware corporation (together with our subsidiaries, "we," "our," "Abeona" or the "Company"), is a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases. Our lead clinical programs consist of: (i) EB-101, an autologous, gene-corrected cell therapy for recessive dystrophic epidermolysis bullosa ("RDEB"), (ii) ABO-102, an adeno-associated virus ("AAV")-based gene therapy for Sanfilippo syndrome type A ("MPS IIIA"), and (iii) ABO-101, an AAV-based gene therapy for Sanfilippo syndrome type B ("MPS IIIB"). We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases and next-generation AAV-based gene therapies using the novel AIM™ capsid platform that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs. Our product candidates are eligible for orphan drug designation, breakthrough therapy designation, or other expedited review processes in the U.S., Europe, Japan, or other world markets. Our pipeline includes three programs in clinical development—EB-101, ABO-101 and ABO-102— for which we hold several U.S. and European Union ("EU") regulatory designations, and a pipeline of additional earlier stage programs:

Our robust pipeline features early- and late-stage candidates with the potential to transform the treatment of devastating genetic diseases, and we are conducting clinical trials in the U.S. and abroad.

Our Mission and Strategy

Abeona is at the forefront of gene and cell therapy research and development. We are a fully-integrated company featuring therapies in clinical development, in-house manufacturing facilities, a robust pipeline, and scientific and clinical leadership. We see our mission as working to create, develop, manufacture, and deliver gene and cell therapies for people impacted by serious diseases. We partner with leading academic researchers, patient advocacy organizations and caregivers to develop therapies that address the underlying cause of a broad spectrum of rare genetic diseases for which no effective treatment options exist today.

Since our last fiscal year, we have continued to make progress toward fulfilling our goal of harnessing the promise of genetic medicine to transform the lives of people impacted by serious diseases and redefining the standard of care through gene and cell therapies. Our strategy to achieve this goal consists of:

Advancing our Clinical Gene and Cell Therapy Programs and Research and Development with a Focus on Rare and Orphan Diseases.

We have three programs in clinical development—EB-101, ABO-101 and ABO-102—and a pipeline of additional earlier stage programs. Through our gene and cell therapy expertise in research and development, we believe we are positioned to introduce efficacious and safe therapeutics to transform the standard of care in devastating diseases and establish our leadership position in the field.

Applying Novel Next-Generation AIM™ Capsid Technology to Develop New In-Vivo Gene Therapies.

We are researching and developing next-generation AAV-based gene therapy using our novel capsids developed from the AIM™ Capsid Technology Platform and additional Company-invented AAV capsids. We plan to continue to develop chimeric AAV capsids capable of improved tissue targeting for various indications and potentially evading immunity to wildtype AAV vectors.

Establishing Leadership Position in Commercial-Scale Gene and Cell Therapy Manufacturing.

We established current Good Manufacturing Practice ("cGMP"), clinical-scale manufacturing capabilities for gene-corrected cell therapy and AAV-based gene therapies in our state-of-the-art Cleveland, OH facility. We believe that our platform provides us with distinct advantages, including flexibility, scale, reliability, and the potential for reduced development risk, reduced cost, and faster times to market. We have focused on establishing internal Chemistry, Manufacturing and Controls ("CMC") capabilities that drive value for our organization through process development, assay development and manufacturing. We have also deployed robust quality systems governing all aspects of product lifecycle from preclinical through commercial stage.

Establishing Additional Gene and Cell Therapy Franchises and Adjacencies through In-Licensing and Strategic Partnerships.

We seek to be the partner of choice in gene therapy disease treatment and have closely collaborated with leading academic institutions, key opinion leaders, patient foundations, and industry partners to generate novel intellectual property, accelerate research and development, and understand the needs of patients and their families.

Maintaining and Growing IP Portfolio.

We strive to have a leading intellectual property portfolio. To that end, we seek patent rights for various aspects of our programs, including vector engineering and construct design, our production process, and all features of our clinical products including composition of matter and method of administration and delivery. We expect to continue to expand our intellectual property portfolio by aggressively seeking patent rights for promising aspects of our product engine and product candidates.

Our Pipeline

Our robust pipeline features early- and late-stage candidates with the potential to transform the treatment of devastating genetic diseases, and we are conducting clinical trials in the U.S. and abroad.

Our lead clinical programs consist of: (i) EB-101, an autologous, gene-corrected cell therapy for RDEB, (ii) ABO-102, an AAV-based gene therapy for MPS IIIA and (iii) ABO-101, an AAV-based gene therapy for MPS IIIB. We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases and next-generation AAV-based gene therapies using the novel AIM™ capsid platform that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs.

Developing Next Generation Gene and Cell Therapy

EB-101 for the Treatment of Recessive Dystrophic Epidermolysis Bullosa ("RDEB")

Disease Overview

RDEB belongs to a group of genetic skin disorders known more broadly as epidermolysis bullosa. Patients with RDEB have a defect in the COL7A1 gene, resulting in the inability to produce Type VII collagen, which plays a vital role in anchoring the skin's dermal and epidermal layers.

RDEB patients have fragile skin, which can easily damage to produce open and blistering wounds, disfiguring scars throughout the body, fused fingers and toes, limits in range of motion at joints (e.g., arms and legs), and an abnormal narrowing of the esophagus. Long-term RDEB patients can suffer from anemia, are at high risk of developing aggressive squamous cell carcinomas, infections, and premature death. The most severe patients are approximately 20 times more likely to die by 30 years of age than the general population.

Similar to most ultra-rare diseases, the incidence and prevalence of RDEB are not well defined. Incidence of 0.2 to 3.05 per million births and prevalence of 0.14 to 1.35 per million people have been observed across different geographies, primarily estimated by limited population analyses of clinical databases or registries (Eichstadt et al.; Clinical, Cosmetic and Investigational Dermatology, 2019). Using genetic modeling of COL7A1 variants, which is believed to cause RDEB, Stanford University estimated the incidence of RDEB to be approximately 63 per million births and prevalence could be up to 3,850 patients in the U.S., whose wounds may benefit from COL7A1-mediated treatments such as EB-101.

RDEB patients have, on average, 11 active wounds on their bodies, with the majority > 20 cm2 (Stanford University; Solis, D., et al., 2017). In 2020, a survey of RDEB patients reported that approximately 60% have active wounds covering greater than 30% of their bodies (Bruckner et al.; Orphanet Journal of Rare Diseases, 2020). Wounds covering up to approximately 80% of body surface area have been recorded in some EB patients (Hirsch et al.; Nature Research, 2017).

We expect EB-101 could be a treatment option for all RDEB wounds and specifically target larger and/or chronic wounds for which EB-101 has shown durable healing and associated pain reduction in a phase 1/2 clinical trial. The data from the phase 1/2 clinical trial supports the VIITAL™ phase 3 trial. These larger and/or chronic wounds carry the highest burden, including the need for frequent dressing changes, pain, pruritus, risk of infection, and developing skin cancer.

Current Management of RDEB

At present, there are no approved treatments for RDEB in the U.S. or Europe.

Wound management currently consists of supportive care to limit contamination and infection, and reduction in mechanical forces that produce new blisters. Care usually includes treatment of new blisters by lancing and draining. Wounds are then dressed with a non-adherent material, covered with padding for stability and protection, and secured with an elastic wrap for integrity. The estimated annual cost of wound dressings alone for an RDEB patient can range from $245,000 per year to significantly higher in more severe cases.

RDEB patients also have periodic surgeries to relieve disease related issues such as narrowing of their esophagus, fusing of fingers and corneal abrasions.

Program Status

EB-101 is an autologous, gene-corrected cell therapy in which a functioning COL7A1 gene is inserted into a patient's own skin cells (keratinocytes) using a retrovirus. The keratinocytes are then transplanted back to the patient to restore Type VII collagen expression and skin function.

EB-101 has been granted Regenerative Medicine Advanced Therapy ("RMAT"), Breakthrough Therapy, Rare Pediatric Disease, and Orphan Drug designations by the U.S. Food and Drug Administration ("FDA"); as well as Orphan Drug designation by the European Medicines Agency ("EMA").

Results from a completed Phase 1/2 study that enrolled 7 patients with large and chronic RDEB wounds at Stanford University showed that EB-101 was well-tolerated and resulted in significant and durable wound healing (Siprashvili, Z., et al., 2016), with up to seven years of follow-up (Eichstadt, S., et al. JCI Insight 2019). To date, there have been no reported serious adverse events.

In 2020 Abeona initiated a pivotal Phase 3 clinical trial, referred to as VIITAL™, evaluating the potential of EB-101 for the treatment of RDEB. VIITAL™ is an ongoing randomized, control-matched Phase 3 clinical trial assessing treatment with EB-101 in 10 to 15 patients, comprising 35 large chronic wound sites treated in total. The co-primary endpoints of VIITAL™ are a) proportion of EB-101 treated wounds with >50% healing from baseline at 24 weeks and b) improvement in pain at 24 weeks assessed by the Wong-Baker pain scale at time of dressing change versus an untreated control wound. The FDA has agreed on endpoints and other characteristics of the study.

ABO-102 and ABO-101 for the treatment of Mucopolysaccharidosis (MPS) III (Sanfilippo syndrome)

Disease Overview

MPS III (Sanfilippo syndrome) is a group of four inherited lysosomal storage diseases, described as type A, B, C or D, which result from enzyme deficiencies responsible for abnormal accumulation of glycosaminoglycans ("GAGs"), which are long, linear polysaccharides also known as mucopolysaccharides, in body tissues that lead to progressive cell damage and neurodevelopmental and physical decline. The incidence of MPS III (all four types combined) is estimated to be 1 in 70,000 births.

Lysosomes are intra-cellular structures responsible for a continuous process of replacing used materials and breaking them down for disposal. Children with MPS III are missing a lysosomal enzyme that is essential in breaking down used mucopolysaccharides, specifically heparan sulfate. The partially broken down heparan sulfate remains stored in cells in the body causing progressive lysosomal and cell damage and eventually cell death. Babies may show little sign of the disease early in life, but as neurodevelopment is impaired and more cells become damaged, symptoms start to appear within the first few years of life.

In MPS III, the predominant symptoms are speech/language delay, cognitive decline, behavioral abnormalities, motor dysfunction, and seizures, eventually leading to premature death. Most patients with the rapidly progressing form of MPS III do not reach a level of cognitive function above that of an unaffected three-year-old child. Accumulation of heparan sulfate and related cell dysfunction also affects other organs, leading to liver enlargement and soft tissue coarsening. To date, there is no cure for MPS III and care is only supportive and palliative.

Program Status

We are developing AAV-based gene therapies ABO-102 and ABO-101 for MPS IIIA and MPS IIIB (Sanfilippo syndrome Type A and Sanfilippo syndrome Type B), respectively. These gene therapies are administered once through intravenous infusion. ABO-102 and ABO-101 deliver a functioning copy of the defective gene to cells of the central nervous system ("CNS") and peripheral organs with the aim of halting the deleterious effects caused by the malfunctioning enzyme and impairment of lysosomal functioning. Both viral vector constructs rely on the neurotropism of the AAV9 serotype and its ability to cross the blood brain barrier ("BBB") and deliver the functional copy of the gene to the CNS.

ABO-102 for MPS IIIA

Preclinical *in vivo* efficacy studies in animals with MPS IIIA showed that a single dose of ABO-102 significantly restored cell and organ function, corrected neurological deficits, increased motor control, and increased the lifespan by more than 100% one year after treatment compared with untreated control animals. In addition, safety studies conducted in animal models of MPS IIIA demonstrated that delivery of ABO-102 was well-tolerated with minimal side effects. ABO-102 received Fast Track and RMAT designations by the FDA, PRIME designation in the EU, Orphan Drug designations in the U.S. and EU, and FDA Rare Pediatric Disease designation.

On February 12, 2021, we reported updated data from the ongoing Phase 1/2 gene transfer clinical trial of ABO-102 (scAAV9.U1a.hSGSH) for Mucopolysaccharidosis IIIA, or MPS IIIA, (study ABT-001; NCT02716246). MPS IIIA is caused by the absence of functional SGSH gene. In the trial, subjects receive a single intravenous injection of ABO-102 to facilitate systemic delivery, including to the CNS, of a functional SGSH gene. Subjects are evaluated at multiple time points post-treatment for safety and signals of biopotency and clinical efficacy. The results to-date from the high dose cohort 3 (currently enrolling) showed evidence of preservation of neurocognitive development with continuous cognitive gains within normal range of a non-afflicted child, for 2.5 years to 3 years after treatment with ABO-102 in the three young patients treated before 30 months of age with relevant follow-up, as well as dose-related and sustained reduction in cerebrospinal fluid ("CSF") levels of heparan sulfate, denoting transgene expression in the CNS, and a durable reduction of liver volume. No treatment related serious adverse events ("SAEs") have been reported to date, with follow-up longer than two years post treatment in the majority of patients.

Summary of MPS IIIA ABO-102 Phase 1/2 Study Data:

- 19 patients treated as of January 2021
- Clear dose-response and sustained reduction of heparan sulfate levels in CSF
- Sustained reduction in liver volume
- Positive neurocognitive signals seen in younger, higher functioning patients enrolled in cohort 3
- As of January 2021, mean follow-up in cohort 1 (55 months); cohort 2 (47 months); and cohort 3 (24 months):
    - ABO-102 has been well tolerated to date
    - No deaths
    - No infusion-related adverse events
    - No serious drug-related adverse events
    - ELISpot negative for the SGSH enzyme

We have initiated a second Phase 1/2 clinical trial with ABO-102 (study ABT-003; NCT04088734) to treat patients who do not qualify for participation on study ABT-001 because of their more advanced cognitive impairment caused by MPS IIIA. The first patient in study ABT-003 was enrolled in 2019 at Adelaide Women's and Children's Hospital in Australia and two more patients were enrolled in Spain in 2020. We initiated this clinical trial in the U.S. in early 2021.

ABO-101 for MPSIIIB

Preclinical *in vivo* efficacy studies in mice with MPS IIIB showed that a single dose of ABO-101 significantly restored cell and organ function, corrected neurological deficits, increased neuromuscular control, and normalized lifespan compared with untreated control animals. In addition, safety studies conducted in MPS IIIB mice and wildtype mice, and in non-human primates, demonstrated that systemic delivery of ABO-101 was well tolerated with minimal side effects.

In the ABO-101 (rAAV9.CMV.hNAGLU) program for Mucopolysaccharidosis IIIB (MPS IIIB), subjects in our ongoing Phase 1/2 gene transfer clinical study (study ABT-002; NCT03315182) receive a single, intravenous infusion of ABO-101, which uses an AAV9 vector to introduce a functional NAGLU gene to treat patients with MPS IIIB disease. Subjects are evaluated at multiple time points post-injection for safety assessments and efficacy parameters. On February 12, 2021, we reported updated data from the ABT-002 trial showing dose dependent increases in plasma NAGLU activity, with normalization up to 6 months in cohort 3, accompanied by dose-dependent reductions of plasma and urinary heparan sulfate and urinary GAGs and decreased CSF levels of heparan sulfate levels sustained up to 24 months in the patient in Cohort 1 that reached that timepoint. Longer follow-up in patients treated in cohorts 2 and 3 is needed to address cognitive changes. There was one serious drug-related adverse event of prolonged hospitalization reported in cohort 3 where the patient experienced a grade 2 episode of diarrhea and vomiting after treatment with ABO-101 and was required to stay in the hospital for two additional days for observation.

As of February 2021, the clinical trial is ongoing in the U.S., Spain, Germany, and France.

Summary of MPS IIIB ABO-101 Phase 1/2 Study Data:

- 11 patients treated as of January, 2021
- Clear signals of biologic effect with reduction of disease-specific biomarkers in the CSF, plasma and urine and reduction in liver volumes
- Longer follow-up in patients treated in Cohorts 2 and 3 is needed to address cognitive changes
- As of January 2021, mean follow-up in cohort 1 (31 months), cohort 2 (17 months) and cohort 3 (7 months):
    - ABO-101 has been well tolerated to date
    - No deaths
    - No infusion-related adverse events
    - One serious drug-related adverse event requiring two additional days of hospitalization for observation due to a grade 2 episode of diarrhea and vomiting
    - ELISpot negative for the NAGLU enzyme

ABO-50X for the treatment of genetic eye disorders

Program Overview

This research program comprises several vectors being tested for different monogenic retinal disorders. Eighty percent of genetic eye disorders affect the photoreceptor cells, and correction of mutations in the retina has been accomplished by several groups using AAV gene therapy delivered through subretinal injection. We are exploring various routes of administration to deliver AAV to the retina, including intravitreal and para-retinal delivery. We believe intravitreal delivery of small volume gene therapies is an attractive alternative to deliver gene therapy to the retina in an out-patient setting. We anticipate para-retinal injection to be safer as compared to subretinal and may serve programs that currently require subretinal dosing.

Program Status

In a preclinical study, we noted that intravitreal administration of the novel AIM™ AAV204 capsid in non-human primates resulted in broad transgene expression in the peripheral retina as well as intense expression in the fovea 25 days post-administration. AAV204 also transduced photoreceptor cells in retinal explants and transduced the outer retina, with positive green fluorescent protein expression.

The non-human primate data were complemented by findings from mice models, which identified AAV204 as one of three lead candidate AIM™ capsids that demonstrate robust transduction of retinal cells. The data in mice demonstrated that intravitreal administration resulted in broad retinal expression of AAV204 that penetrated to the photoreceptor and retinal pigmented epithelium layers.

ABO-201 for the treatment of CLN3 disease, also known as juvenile Batten disease (or Juvenile Neuronal Ceroid Lipofuscinosis) ("CLN3 Disease")

Disease Overview and Program Overview

CLN3 disease is a rare, fatal, autosomal recessive (inherited) disorder of the nervous system that typically begins between 4 and 8 years of age. Often the first noticeable sign of CLN3 disease is vision impairment, which tends to progress rapidly and eventually result in blindness. As the disease progresses, children experience loss of previously acquired skills (developmental regression). This regression usually begins with the loss of the ability to speak in complete sentences. Children then lose motor skills, such as the ability to walk or sit. They also develop movement abnormalities that include rigidity or stiffness, slow or diminished movements (hypokinesia), and stooped posture. Beginning in mid-to-late-childhood, affected children may have recurrent seizures (epilepsy), heart problems, behavioral problems, and difficulty sleeping. Normal life expectancy is greatly reduced. Most people with juvenile Batten disease live into their twenties or thirties. As of December 31, 2020, no specific treatment is known that can halt or reverse the symptoms of CLN3 disease.

ABO-201 (scAAV9.CLN3) is an AAV-based gene therapy that has shown preclinical efficacy following delivery of a functioning copy of the CLN3 gene to a mouse model of CLN3 disease. Preclinical studies have previously demonstrated reduced lysosomal storage and decreased astrocyte/microglia activation in the CNS as well as improved motor function.

ABO-401 for the Treatment of Cystic Fibrosis

Disease Overview and Program Overview

Cystic Fibrosis ("CF") is a progressive genetic disorder caused by a mutation in the cystic fibrosis transmembrane conductance regulator ("CFTR") gene. Malfunction of this gene affects cells that produce mucus, sweat and digestive juices. In unaffected individuals, these secreted fluids are normally thin and slippery, but in cystic fibrosis, a defective gene causes the secretions to become sticky and thick. Instead of acting as a lubricant, the secretions plug up tubes, ducts, and passageways, especially in the lungs and pancreas, and cause repeated lung infections and difficulty breathing, and impaired pancreas function and digestive abnormalities.

The preclinical ABO-401 program employs the AAV204 AIM^{TM} capsid. ABO-401 has shown the ability to deliver the CFTR transgene to the lungs of gut-corrected delta-F508 mice. Another study also demonstrated CFTR transgene expression that has corrected the underlying chloride current deficit in human CF donor derived nasal and bronchial epithelium cells grown at the air-liquid interface and treated with ABO-401. Correction of chloride channel current following ABO-401 administration occurred regardless of underlying mutations of the CF transmembrane conductance regulators, including the most common CF mutation, delta-F508.

Next-Generation Gene Therapy Treatments anchored in AIM™ Vector Platform

In 2016, we licensed a library of first-generation novel AAV capsids from the University of North Carolina at Chapel Hill. In partnership with academic institutions, our own scientific research teams have identified vectors within the AIM™ capsid library showing strong potential to successfully target and reach the central nervous system, lung, muscle, liver, and other tissues. Based on continuing research being conducted by Abeona and our research partners, we observed improvements in gene delivery to specific tissues compared to currently available AAV technology. We believe AIM™ vectors also have the potential for redosing subjects who previously received certain AAV gene therapy or subjects who have pre-existing antibodies to naturally occurring AAV serotypes.

Establishing Leadership Position in Commercial-Scale Gene and Cell-Therapy Manufacturing

We have established a cGMP manufacturing facility, the Elisa Linton Center located in Cleveland, Ohio, which enables us to enhance supply chain control, establish tighter quality control testing, increase supply capacity, reduce production costs and gain manufacturing efficiency for clinical trials related to our product candidates and ensure commercial demand is met in the event our therapies receive marketing approval. Our facility is led by a team of highly-skilled production, process/assay development and QA/QC scientists with expertise in gene and cell therapy, particularly in cell culture, formulation, upstream, downstream and purification manufacturing. We have completed the first two phases of our 26,000+ square foot manufacturing build-out plans in Cleveland, Ohio. The first phase, completed in 2018, was a 6,000 square foot state-of-the-art cGMP production facility for the manufacturing of gene and cell therapies. The facility is designed to initially manufacture clinical drug products with later intent of manufacturing commercial grade cGMP drug product. The second phase, completed in 2019, was the completion of an additional 8,000 square feet of state-of-the-art laboratory space to support our expanding quality control and process development, and assay development teams. The second phase also included nearly 2,000 square feet of cGMP Inventory Control space. The last phase of our manufacturing build-out plan would be a clinical/commercial AAV facility to support manufacturing to meet anticipated product demand globally.

We have advanced our in-house manufacturing capabilities for our autologous cell replacement therapy (EB-101) for the treatment of RDEB. The product is manufactured as a multilayer cellular sheet containing corrected keratinocytes that is fastened to a petrolatum gauze backing with surgical hemoclips. It is applied over wound areas, where they are expected to produce keratinocytes with functioning Type VII collagen, providing wound coverage and allowing for long-term wound healing. A key component to the EB-101 drug product manufacturing process is the retroviral vector which delivers the functional copy of the Collagen VII Alpha 1 cDNA to the autologous patient cells. We have developed the cGMP manufacturing process for the LZRSE-Col7A1 retroviral vector and have produced three GMP lots for analytical and clinical comparability. We have developed a GMP master cell bank and a working cell bank to support the GMP production of the retroviral vector.

We are developing AAV vector manufacturing capabilities that use the triple plasmid transient transfection method. We insert, or transfect, many copies of three DNA plasmids encoding the specific therapeutic gene sequence, or transgene, the capsid coding sequence, and helper sequences into AAV-293 cells using a serum-free, suspension bioreactor vector production technology. During an incubation period following transfection, each cell produces AAV vectors through biosynthesis using the cells' natural machinery. At the end of the incubation period, the newly generated AAV vectors are harvested, then purified and filtered in a multi-step process. We continue to maintain focus on cGMP compliance and ensuring adequate supply to support our future clinical activity.

We have established and maintained strong and collaborative relationships with third-party companies specializing in the testing of gene and cell therapy material to complement our process and assay development needs.

We have made significant investments in developing optimized manufacturing processes and believe that our processes and methods developed to date provide a comprehensive manufacturing process for EB-101 and AAV-based vector therapies, including:

- sufficient scale to support commercial manufacturing requirements for EB-101
- processes related to biopsy, cell collection, storage and transportation as part of manufacturing for EB-101
- processes related to product release testing for EB-101
- processes related to the manufacture of retroviral supernatant
- establishing transportation and packaging processes and materials for finished EB-101 product
- proprietary AAV vector manufacturing processes and techniques that produce a highly purified product candidate
- AAV serum-free suspension technology that is readily scalable
- multiple assays to accurately characterize our process and the AAV vectors we produce
- a series of purification processes, which may be adapted and customized for multiple different AAV capsids, with a goal of higher concentrations of active vectors, and that are essentially free of empty capsids.

We believe that these improvements and our continued investment in our manufacturing platform will enable us to develop best-in-class, next-generation gene and cell therapy products. As we look to commercialize EB-101, we are working towards filing a Biologics License Application ("BLA") to support commercial manufacturing of EB-101 from our Cleveland facility.

Maintain a Strong Intellectual Property Portfolio

We strive to protect our commercially important proprietary technology, inventions, and know-how, including by seeking, maintaining, and defending patent rights, both for inventions developed internally and for inventions licensed from third parties. We also rely on trade secrets and know-how relating to our proprietary technology platforms, continuing technological innovation, and in-licensing opportunities to develop, strengthen and maintain our position in the field of gene and cell therapy. We may also rely on regulatory protection afforded through data exclusivity, market exclusivity, and patent term extensions where available.

Our success may depend in part on our ability to obtain and maintain patent and other protections for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and intellectual property rights of third parties. Our ability to stop third parties from making, having made, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third-party licensors. With respect to both licensed and company-owned intellectual property, we may not be granted patents with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We are actively seeking U.S. and international patent protection for a variety of technologies, including the following: research tools and methods, methods for transferring genetic material into cells, AAV-based biological products, methods of designing novel AAV constructs, methods for treating diseases of interest and methods for manufacturing, packaging, and transporting our product candidates. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel biological products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various license agreements that give us rights to use specific technologies in our research and development, and future commercialization.

Licensed Technologies and Intellectual Property

1. ***Mucopolysaccharidosis ("MPS") IIIA and IIIB***

We have secured an exclusive license through Nationwide Children's Hospital to a family of patent applications for AAV-based treatments for patients with MPS IIIA and IIIB. The family includes three pending applications in the United States. United States patent(s) that may grant from this family would be expected to expire in approximately 2031 and 2032.

2. ***CLN3 Disease (Juvenile Batten Disease)***

We have licensed exclusive rights to an international patent family from the University of Nebraska Medical Center and the Ohio State Innovation Foundation, directed to AAV gene therapy for the treatment of CLN3 disease (also known as juvenile Batten disease). The licensed patent family includes pending national stage applications in the United States, Canada, Europe, China, Japan, New Zealand, and Australia, as well as U.S. Patent No. 10,876,134 ("the '134 Patent"), entitled "Gene therapy for juvenile batten disease," which was issued on December 29, 2020 and contains claims directed to CLN3-related vectors, methods, and formulations. The '134 Patent is expected to expire in December 2035 absent any future grant of patent term extension.

3. Recessive Dystrophic Epidermolysis Bullosa

To support our EB franchise, we have licensed a patent family from Stanford University covering technology for the treatment of RDEB. National stage patent applications are pending in the United States, Canada, Europe, Israel, Japan, South Korea, China, New Zealand, Australia, Russia, Mexico, South Africa, and Brazil. United States patent(s) that may grant from this portfolio would be expected to expire in approximately 2037. We have also filed a United States provisional patent application directed to packaging and transport of the EB product.

4. AIM™ Capsids

We have an exclusive license to an international patent family from UNC at Chapel Hill covering novel adeno-associated virus ("AAV") capsids ("AIM™ capsids") that may potentially be used to deliver a wide variety of therapeutic transgenes to human cells to treat genetic diseases. National stage applications directed to the AIM™ capsids have been filed in the United States, Australia, Brazil, China, Hong Kong, Europe, Canada, Israel, India, Japan, South Korea, Mexico, New Zealand, Russia, and South Africa. The first patent in this patent family, U.S. Patent No. 10,532,110 (the "'110 Patent"), issued to UNC on January 14, 2020. The '110 Patent is entitled to 352 days of patent term adjustment, making its projected expiration date November 6, 2036. The second patent in this patent family, U.S. Patent No. 10,561,743 (the "'743 Patent"), issued to UNC on February 18, 2020. The '743 Patent is expected to expire on November 20, 2035. We have exclusive rights to both the '110 Patent and the '743 Patent under our license with UNC.

5. CLN1 Disease (Infantile Batten Disease)

We have also licensed from UNC at Chapel Hill rights to a patent portfolio directed to optimized CLN1 genes and expression cassettes for use in treating CLN1 disease (also known as infantile Batten disease). Patent applications are pending in the United States, Canada, Europe, Israel, India, China, Japan, South Korea, Australia, New Zealand, Mexico, Brazil, Russia, and South Africa. United States patent(s) that may grant from this portfolio would be expected to expire approximately in 2037. In August 2020, we entered into an agreement exclusively sublicensing the CLN1 patent portfolio to Taysha Gene Therapies.

6. Rett Syndrome

We have licensed rights to patent applications from both UNC at Chapel Hill and the University of Edinburgh relating to gene therapy for the treatment of Rett Syndrome. The patent applications licensed from UNC at Chapel Hill are directed to viral genomes designed to regulate expression of the MeCP2 gene, which is mutated in patients with Rett Syndrome. The patent applications licensed from the University of Edinburgh are directed to expression cassettes for MeCP2 polypeptides and to synthetic MeCP2 polypeptides. National stage applications for the patent application directed to MeCP2 expression cassettes are now pending in the United States, Canada, Brazil, China, Japan, Australia, Europe, India, South Korea, and Russia, and national stage applications for the international application directed to synthetic polypeptides are currently pending in the United States, Canada, Brazil, China, and Japan. In October 2020, we entered into an agreement exclusively sublicensing these UNC and Edinburgh patent rights to Taysha Gene Therapies.

We will explore in due course strategies to support patent term extensions for all of our licensed portfolios.

U.S. Biologic Products Development Process

In the United States, the FDA regulates biologic products including gene therapy products under the Federal Food, Drug, and Cosmetic Act ("FDCA"), the Public Health Service Act ("PHSA"), and regulations implementing these laws. The FDCA, PHSA and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, advertising, and promotion of biologic products. Applications to the FDA are required before conducting human clinical testing of biologic products. FDA approval also must be obtained before marketing of biologic products. Gene therapy studies may also need to comply with the National Institutes of Health ("NIH") Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"), which includes additional requirements, such as the review and approval of the study by an Institutional Biosafety Committee. Moreover, in light of the COVID-19 pandemic, the FDA has issued a number of guidance documents to assist companies navigating COVID-19, product development, and manufacturing, including guidance specific to gene therapies.

Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Tissues and Advanced Therapies ("OTAT") and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee ("CTGTAC"), a panel of medical and scientific experts and consumer representatives, to advise CBER on its reviews. The FDA has issued a growing body of guidance documents on chemistry, manufacturing, and control ("CMC"), clinical investigations and other areas of gene therapy development, all of which are intended to facilitate the industry's development of gene therapy products.

The process required by the FDA before a biologic product candidate may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and in vivo studies in accordance with the FDA's current Good Laboratory Practice ("GLP") regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an Investigational New Drug Application ("IND"), which allows human clinical trials to begin unless the FDA objects within 30 days;
- approval by an independent institutional review board ("IRB"), reviewing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's Good Clinical Practice ("GCP") regulations, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biologic product candidate for its intended use;
- development of manufacturing processes to ensure the product candidate's identity, strength, quality, purity, and potency;
- preparation and submission to the FDA of a BLA for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the biologic product candidate is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biologic product candidate's identity, safety, strength, quality, potency and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- payment of user fees and the FDA review and approval, or licensure, of the BLA. BLA application fees for products designated as orphan drugs by the FDA are waived.

Before testing any biologic product candidate on humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity, and formulation, as well as in vivo studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, the study must also comply with the NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA. However, many companies and other institutions, not otherwise subject to the NIH Guidelines, voluntarily follow them.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not commence or recommence without FDA authorization and then only under terms authorized by the FDA.

Human clinical trials under an IND

Clinical trials involve the administration of the biologic product candidate to healthy volunteers or patients under the supervision of qualified investigators, which generally are physicians not employed by, or under the control of, the trial sponsor. Investigators must also provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent.

Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers items such 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 communications to study subjects before a study commences at that site and the form and content of the informed consent that must be signed by each clinical trial subject, or his or her legal representative, and must monitor the clinical trial until completed. Clinical trials involving recombinant DNA also must be reviewed by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees basic and clinical research that utilizes recombinant DNA at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Information about certain clinical trials, including a description of the study and study results, must be submitted within specific timeframes to NIH for public dissemination on their clinicaltrials.gov website. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions must also have a publicly available policy on evaluating and responding to requests for expanded access requests.

Investigational biologics and therapeutic substances imported into the United States are also subject to regulation by the FDA. Further, the export of investigational products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

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

- Phase 1: The biologic product candidate initially is introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early understanding of its effectiveness. In the case of some product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2: The biologic product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- Phase 3: The biologic product candidate is administered to an expanded patient population at geographically dispersed clinical trial sites in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for product labeling. Typically, two Phase 3 trials are required by the FDA for product approval. Under some limited circumstances, however, the FDA may approve a BLA based upon a single Phase 3 clinical study plus confirmatory evidence or a single large multicenter trial without confirmatory evidence.

Additional kinds of data may also help to support a BLA, such as patient experience data. Real world evidence may also support a BLA, and, for appropriate indications sought through supplemental BLAs, data summaries may provide marketing application support. For genetically targeted products and variant protein targeted products intended to address an unmet medical need in one or more patient subgroups with a serious or life threatening rare disease or condition, the FDA may allow a sponsor to rely upon data and information previously developed by the sponsor or for which the sponsor has a right of reference, that was submitted previously to support an approved application for a product that incorporates or utilizes the same or similar genetically targeted technology or a product that is the same or utilizes the same variant protein targeted drug as the product that is the subject of the application.

Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be conducted or may be required by FDA after initial approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA

Written IND safety reports must be promptly submitted to the FDA, IRBs, IBCs, and the investigators for serious and unexpected adverse events; any findings from other trials, in vivo laboratory tests or in vitro testing that suggest a significant risk for human subjects; any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure, or other safety information. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

The FDA, the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biologic product candidate has been associated with unexpected serious harm to patients. The FDA or an IRB may also impose conditions on the conduct of a clinical trial.

Additional regulation for gene therapy clinical trials

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND application; the proper design of tests to measure product efficacy in support of an IND or BLA application; and long term patient and clinical study subject follow up and reporting requirements. The FDA has also issued draft guidance specific to the development of gene therapy products for neurodegenerative diseases as such products may face special challenges related to CMCs and clinical and preclinical development, due to the nature of the products and potential patient population (e.g., children), the heterogeneity of neurodegenerative disorders, the route of administration, the volume of the product that can be administered, the delivery device, and the study population size.

Compliance with cGMP requirements

Manufacturers of biologics must comply with applicable cGMP regulations for both clinical and commercial supply. Manufacturers and others involved in the manufacture and distribution of such products at the commercial stage also must register their establishments with the FDA and certain state agencies and list the manufactured products. Recently, the information that must be submitted to FDA regarding manufactured products was expanded through the Coronavirus Aid, Relief, and Economic Security, or CARES, Act to include the volume of drugs produced during the prior year. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Establishments may be subject to periodic, unannounced inspections by government authorities to ensure compliance with cGMP requirements and other laws. Discovery of problems may result in a government entity placing restrictions on a product, manufacturer, or holder of an approved BLA, and may extend to requiring withdrawal of the product from the market. The FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMP requirements and are adequate to assure consistent production of the product within required specification.

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

U.S. review and approval processes

The results of the preclinical tests and clinical trials, together with detailed information relating to the product's CMC and proposed labeling, among other things, are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications.

For gene therapies, selecting patients with applicable genetic defects is a necessary condition to effective treatment. For the therapies we are currently developing, we believe that diagnoses based on symptoms, in conjunction with existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments ("CLIA"), are sufficient to select appropriate patients and will be permitted by the FDA. For future therapies, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to select patients or to assure the safe and effective use of therapies in appropriate patients. The FDA refers to such tests as in vitro companion diagnostic devices and the combination of the in vitro companion diagnostic device and the therapeutic would be considered to be a combination product.

The use of the two products together must be shown to be safe and effective for the proposed intended use and the labeling of the two products must reflect their combined use. In some cases, the device component may require a separate premarket submission; for example, when the device component is intended for use with multiple drug products. Sponsors of clinical studies using investigational devices are required to comply with FDA's investigational device exemption regulations. Once approved or cleared, the sponsor of the device component submission (or the combination product submission, if both components are covered by one premarket submission) would need to comply with FDA's post-market device requirements, including establishment registration, device listing, device labeling, unique device identifier, quality system regulation, medical device reporting, and reporting of corrections and removals requirements.

FDA has a policy position that, when safe and effective use of a therapeutic product depends on a diagnostic device, the FDA generally will require approval or clearance of the diagnostic device at the same time that the FDA approves the therapeutic product. The type of premarket submission required for a companion diagnostic device will depend on the FDA classification of the device. A premarket approval, or PMA, application is required for high risk devices classified as Class III; a 510(k) premarket notification is required for moderate risk devices classified as Class II; and a *de novo* request may be used for novel devices not previously classified by FDA that are low or moderate risk.

FDA may, however, approve a therapeutic product without the concurrent approval or clearance of a diagnostic device when the therapeutic product is intended to treat serious and life-threatening conditions for which no alternative exists and the FDA determines that the benefits from the use of the drug/biologic outweigh the risks from the lack of an approved/cleared companion diagnostic. The FDA would also consider whether additional protections, such as risk evaluation and mitigation strategies, or REMS, or post-approval requirements, are necessary. At this point, it is unclear how the FDA will apply this policy to our gene therapy candidates. Should the FDA deem genetic tests used for selecting appropriate patients for our therapies to be in vitro companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval for a BLA. In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biologic product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biologic product candidate for an indication for which orphan designation has been granted.

Under the Prescription Drug User Fee Act ("PDUFA"), as amended, each BLA must be accompanied by a substantial user fee that must be paid at the time of the first submission of the application, even if the application is being submitted on a rolling basis. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

The FDA reviews a BLA within 60 days of submission to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to accept for filing any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In that event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth, substantive review of the BLA.

The FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and potent, or effective, for its intended use, has an acceptable purity profile and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, safety, strength, quality, potency, and purity. The FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the product candidate. A REMS could include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product candidate is manufactured. The FDA will not approve the product candidate unless it determines that the manufacturing processes and facilities comply with cGMP requirements and are adequate to assure consistent production of the product candidate within required specifications. Additionally, before approving a BLA, the FDA typically will inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements.

On the basis of the BLA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biologic product with specific prescribing information for specific indications. A complete response letter ("CRL") generally outlines the deficiencies in the submission and may require substantial additional testing or information for the FDA to reconsider the application. If a CRL is issued, the applicant may either: resubmit the marketing application, addressing all of the deficiencies identified in the letter; withdraw the application; or request an opportunity for a hearing. If those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter.

If a product candidate receives regulatory approval, the approval may be significantly limited to specific diseases, patient populations, and dosages or the indications for use may otherwise be limited. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling. The FDA also may not approve label statements that are necessary for successful commercialization and marketing. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as Phase IV clinical trials, designed to further assess a biologic product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

The FDA has agreed to specified performance goals in the review of BLAs under the PDUFA. One such goal is to review 90% of standard BLAs in 10 months after the FDA accepts the BLA for filing, and 90% of priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may also be extended if new information is submitted to the application.

Orphan drug designation

Under the Orphan Drug Act, the FDA may designate a biologic product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biologic product available in the United States for treatment of the disease or condition will be recovered from sales of the product). Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan drug designation if there is a product already approved by the FDA that is considered by the FDA to be the same as the already approved product and is intended for the same indication. This hypothesis must be demonstrated to obtain orphan exclusivity. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If granted, prior to product approval, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and certain user-fee waivers. The tax advantages, however, were limited in the 2017 Tax Cuts and Jobs Act. Orphan product designation does not shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, meaning that the FDA may not approve any other applications to market the same drug or biologic product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if the party holding the exclusivity fails to assure the availability of sufficient quantities of the drug to meet the needs of patients with the disease or condition for which the drug was designated. FDA has issued a draft guidance document on how the agency will determine the "sameness" of gene therapy products. Any FDA sameness determinations could impact our ability to receive approval for our product candidates and to obtain or retain orphan drug exclusivity. Competitors additionally may receive approval of different products for the same indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan medicinal product status in the European Union has similar, but not identical, benefits.

Expedited development and review programs

The FDA is authorized to expedite the review of BLAs in several ways. Under the Fast Track program, the sponsor of a biologic product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Biologic products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track BLA before the application is complete, a process known as rolling review. This "rolling review" is available if the applicant provides and the FDA approves a schedule for the remaining information.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- *Breakthrough therapy designation:* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives the following: intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative, and cross-disciplinary review; and rolling review.
- *Priority review:* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious condition compared to marketed products. The FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.
- *Accelerated approval:* Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well-controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug or biologic from the market on an expedited basis.

Fast Track designation, breakthrough therapy 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.

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

Post-approval requirements

Rigorous and extensive FDA regulation of biologic products continues after approval, particularly with respect to cGMP requirements. Manufacturers are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biologic products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse events, reporting updated safety and efficacy information, and complying with electronic record and signature requirements.

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states. After a BLA is approved, the product also may be subject to official lot release. If the product is subject to official lot release by the FDA, the manufacturer submits samples of each lot of product to the FDA, together with a release protocol, showing a summary of the history of manufacture of the lot and the results of all tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biologic products.

There also are continuing annual program user fee requirements for approved products, excluding orphan products. In addition, manufacturers and other entities involved in the manufacture and distribution of approved therapeutics are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMP and other requirements, which impose certain procedural and documentation requirements upon the company and third-party manufacturers.

A sponsor also must comply with the FDA's marketing, advertising, and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company can make only those claims relating to a product that are approved by the FDA. Physicians, in their independent professional medical judgment, may prescribe legally available products for unapproved indications that are not described in the product's labeling and that differ from those tested and approved by the FDA. Biopharmaceutical companies, however, are required to promote their products only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including, but not limited to, criminal and civil penalties under the FDCA and False Claims Act, exclusion from participation in federal healthcare programs, mandatory compliance programs under corporate integrity agreements, suspension and debarment from government contracts, and refusal of orders under existing government contracts.

In addition, the distribution of prescription biopharmaceutical samples is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of samples at the federal level. Both the PDMA and state laws limit the distribution of prescription biopharmaceutical product. Certain reporting related to samples is also required. Free trial or starter prescriptions provided through pharmacies are also subject to regulations under the Medicaid Drug Rebate Program and potential liability under anti-kickback and false claims laws.

Moreover, the enacted Drug Quality and Security Act, or DQSA, imposed obligations on sponsors of biopharmaceutical products related to product tracking and tracing. Among the requirements of this legislation, sponsors are required to provide certain information regarding the products to individuals and entities to which product ownership is transferred, are required to label products with a product identifier, and are required to keep certain records regarding the product. The transfer of information to subsequent product owners by sponsors is also required to be done electronically. Sponsors must also verify that purchasers of the sponsors' products are appropriately licensed. Further, under this legislation manufacturers have product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death. Similar requirements additionally are and will be imposed through this legislation on other companies within the biopharmaceutical product supply chain, such as distributors and dispensers, as well as certain sponsor licensees and affiliates.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Further, should new safety information arise, additional testing or FDA notification may be required. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal actions and adverse publicity. These actions could include refusal to approve pending applications or supplemental applications, withdrawal of an approval, clinical hold, suspension or termination of clinical trial by an IRB, warning or untitled letters, product recalls, adverse publicity, product seizures, total or partial suspension of production or distribution, injunctions, fines or other monetary penalties, refusals of government contracts, mandated corrective advertising or communications to healthcare professionals or patients, exclusion from participation in federal and state healthcare programs, debarment, restitution, disgorgement of profits or other civil or criminal penalties.

U.S. patent term restoration and marketing exclusivity

Depending upon the timing, duration, and specifics of FDA approval of product candidates, some of a sponsor's U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984. The Hatch-Waxman Amendments permit a patent restoration term of up to five years to account for patent term lost during 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 generally is 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. This period may also be reduced by any time that the applicant did not act with due diligence. Only one patent applicable to an approved biologic product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office ("USPTO"), in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Pediatric exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States that, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly responds to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to, and accepted by, the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection that cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve a biosimilar application.

Biosimilars and exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act ("PPACA"), created an abbreviated approval pathway for biologic products shown to be similar to, or interchangeable with, an FDA-licensed reference biologic product, referred to as biosimilars. For the FDA to approve a biosimilar product, it must find that the biosimilar product is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and that there are no clinically meaningful differences between the reference product and proposed biosimilar product. 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 and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. An application for a biosimilar product may not be submitted to the FDA until four years following approval of the reference product, and it may not be approved until 12 years thereafter. These exclusivity provisions only apply to biosimilars—companies that rely on their own data and file a full BLA may be approved earlier than 12 years. Moreover, certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the twelve-year exclusivity period. The PHSA also includes provisions to protect reference products that have patent protection. The biosimilar product sponsor and reference product sponsor may exchange certain patent and product information for the purpose of determining whether there should be a legal patent challenge. Based on the outcome of negotiations surrounding the exchanged information, the reference product sponsor may bring a patent infringement suit and injunction proceedings against the biosimilar product sponsor. The biosimilar applicant may also be able to bring an action for declaratory judgment concerning the patent.

In an effort to increase competition in the biologic product marketplace, Congress, the executive branch, and FDA have taken certain legislative and regulatory steps. For example, in 2020 FDA finalized a guidance to facilitate product importation. Moreover, the 2020 Further Consolidated Appropriations Act included provisions requiring that sponsors of approved biologic products, including those subject to REMS, provide samples of the approved products to persons developing biosimilar products within specified timeframes, in sufficient quantities, and on commercially reasonable market-based terms. Failure to do so can subject the approved product sponsor to civil actions, penalties, and responsibility for attorney's fees and costs of the civil action. This same bill also includes provisions with respect to shared and separate REMS programs for reference and generic drug products.

Rare Pediatric Disease Voucher Program

Under the Rare Pediatric Disease Voucher Program, FDA can award priority review vouchers to sponsors of rare pediatric disease products where the product is intended to treat serious or life-threatening diseases that primarily affect individuals up to age 18. To qualify, the product must contain no active ingredient (including any ester or salt of the active ingredient) that has been previously approved by FDA. The application must also meet other qualifying criteria, including eligibility for FDA priority review. If the necessary qualifying criteria are met, upon a sponsor's request and product approval, FDA may award a priority review voucher. This voucher may be transferred and may be redeemed to receive priority review of a subsequent marketing application for a different product. Use of a priority review voucher is subject to an FDA user fee. As these vouchers are transferable, sponsors may sell these vouchers for substantial sums of money. Vouchers may, however, be revoked by FDA under certain circumstances and sponsors of approved rare pediatric disease products must submit certain reports to FDA. To take advantage of the benefits of this program, the product must be designated by FDA for a rare pediatric disease no later than September 30, 2022, and approved no later than September 30, 2026, unless the law is reauthorized by Congress.

Government regulation outside of the United States

In addition to regulations in the United States, sponsors are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of biologic products. Because biologically-sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not a sponsor obtains FDA approval for a product, a sponsor must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, much like the IND, prior to the commencement of human clinical trials. In the European Union, for example, a request for a Clinical Trial Authorization ("CTA") must be submitted to the competent regulatory authorities and the competent Ethics Committees in the European Union Member States in which the clinical trial takes place, much like the FDA and the IRB, respectively. Once the CTA request is approved in accordance with the European Union and the European Union Member State's requirements, clinical trial development may proceed.

The requirements and processes governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Failure to comply with applicable foreign regulatory requirements may result in, among other things, fines, suspension, variation or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

European Union regulation and exclusivity

To obtain regulatory approval of an investigational biologic product under European Union regulatory systems, applicants must submit a marketing authorization application ("MAA"). The grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products and Regulation (EC) 726/2004 of the European Parliament and of the Council laying down Union procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety and efficacy of their products to the European Medicines Agency ("EMA") which provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Innovative medicinal products are authorized in the European Union based on a full marketing authorization application (as opposed to an application for marketing authorization that relies on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain the results of pharmaceutical tests, preclinical tests and clinical trials conducted with the medicinal product for which marketing authorization is sought. Innovative medicinal products for which marketing authorization is granted are entitled to eight years of data exclusivity. During this period, applicants for approval of generics or biosimilars of these innovative products cannot make an MMA relying on data contained in the marketing authorization dossier submitted for the innovative medicinal product to support their application and such generics or biosimilars cannot be placed on the market until 10 years after the first EU marketing of the reference product. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company, nevertheless, could also market another competing medicinal product for the same therapeutic indication if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Products receiving orphan designation in the European Union can receive 10 years of market exclusivity. During this 10-year period, the competent authorities of the European Union Member States and European Commission may not accept applications or grant marketing authorization for other similar medicinal product for the same orphan indication. There are, however, three exceptions to this principle. Marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- The second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- The holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- The holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

An orphan product can also obtain an additional two years of market exclusivity in the European Union for the conduct of pediatric trials. The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable and no longer justifies the maintenance of market exclusivity or if the manufacturer cannot produce sufficient quantities to supply the orphan population.

The criteria for designating an “orphan medicinal product” in the European Union are similar, in principle, to those in the United States. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan medicinal product designation must be submitted before the application for marketing authorization. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014 (the “Clinical Trials Regulation”), which is set to replace the current Clinical Trials Directive 2001/20/EC (the “Clinical Trials Directive”). The new Clinical Trials Regulation is still pending but implementation is currently expected in December 2021. Until the Clinical Trials Regulation becomes applicable, all clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive, which will be repealed on the day of entry into application of the Clinical Trial Regulation. It will however still apply three years from that day to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opted for the previous system. The Clinical Trial Regulation will overhaul the current system of approvals for clinical trials in the EU. Specifically, the legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the legislation provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications.

In the European Union there are also broadly equivalent regimes for the other issues addressed in relation to US regulation including GMP requirements, accelerated access (generally through so-called Conditional Marketing Authorizations), pediatric requirements and incentives and patent terms restoration (supplementary protection certificates)

Other Healthcare Laws and Regulations

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and use of pharmaceutical products that are granted marketing approval. Arrangements with third-party payors, existing or potential customers and referral sources are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, and these laws and regulations may constrain the business or financial arrangements and relationships through which manufacturers market, sell and distribute the products for which they obtain marketing approval. Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons, and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or kind, in exchange for, or to induce, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers, and formulary managers on the other. Although a number of statutory exemptions and regulatory safe harbors exist to protect certain common activities from falling under the Anti-Kickback Statute, these are narrow, and practices may not fall under the applicable safe harbors and exemptions. For example, HHS recently promulgated a regulation that is effective in two phases. First, the regulation excludes from the definition of "remuneration" limited categories of (a) PBM rebates or other reductions in price to a plan sponsor under Medicare Part D or a Medicaid Managed Care Organization plan reflected in point-of sale reductions in price and (b) PBM service fees. Second, effective January 1, 2023, the regulation expressly provides that rebates to plan sponsors under Medicare Part D either directly to the plan sponsor under Medicare Part D, or indirectly through a pharmacy benefit manager will not be protected under the anti-kickback discount safe harbor. The PPACA amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to commit a violation;
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act (the "FCA"), which prohibit, among other things, individuals, or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payors that are false or fraudulent, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. Certain marketing practices, including off-label promotion, also may implicate the FCA. FCA claims may be pursued by whistleblowers through qui tam actions, even if the government declines to intervene and civil liability may be predicated on reckless disregard for the truth. The PPACA also codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. Separately, the criminal federal False Claims Act imposes criminal fines or imprisonment against individuals or entities who make or present a claim to the government knowing such claim to be false, fictitious, or fraudulent;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS"), information related to payments and other transfers of value made to or at the request of covered recipients, such as, but not limited to, physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family. Payments made to physicians and certain research institutions for clinical trials are included within the ambit of this law. Reported information is made publicly available in searchable formats by CMS;

- additional federal false statements and fraud and abuse statutes prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, a healthcare benefit program, regardless of whether the payor is public or private, in connection with the delivery or payment for health care benefits, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. PPACA amended the intent requirement of certain of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and European Union and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, may be stricter than those applicable in the US and may not have the same effect, thus complicating compliance efforts.

Violation of the laws described above or any other governmental laws and regulations may result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs, debarment from government contracting or refusal of orders under existing contracts, corporate integrity agreements or consent decrees, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly.

Data Privacy and Security

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH Act, and similar state laws impose obligations on certain entities with respect to safeguarding the privacy, security and transmission of protected health information. HIPAA's security and certain privacy standards are directly applicable to persons or organizations of covered entities, other than members of the covered entity's workforce, that create, receive, maintain or transmit protected health information on behalf of a covered entity for a function or activity regulated by HIPAA. The HITECH Act strengthened the civil and criminal penalties that may be imposed against covered entities, business associates and individuals, 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 attorneys' fees and costs associated with pursuing federal civil actions. In addition, other federal and state laws, such as the California Consumer Privacy Act, may regulate the privacy and security of information that we maintain, many of which may differ from each other in significant ways and may not be preempted by HIPAA; and
- the General European Data Protection Regulation, which became applicable May 25, 2018, harmonizes data privacy laws across Europe. This Regulation lays down rules relating to the protection with regard to the processing and transfer of personal data as well as an individual's right to the protection of personal data, including medical information and clinical trial related data. In addition, there are rules relating to the export of personal data outside the European Union and in particular there are certain challenges in relation to export to the United States.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any product candidates for which regulatory approval for commercial sale is obtained will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities and health programs in the United States such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all FDA-approved drugs for a particular indication. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, required disclosures of pricing and sensitive cost data, requirement for payment of manufacturer rebates and negotiation of supplemental rebates, restrictions on reimbursement and requirements for substitution of generic products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies as part of health technology assessment that compare the cost-effectiveness of a particular product candidate to currently available therapies. EU member states may approve a specific price for a product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control company profits. The downward pressure on health care costs has become 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 competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations may not allow favorable reimbursement and pricing arrangements.

Health Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality, or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts. For example, healthcare reform measures under the Affordable Care Act included increased Medicaid rebates, expanded the 340B drug discount program, and changes requiring manufacturer discounts currently set at 70 percent on Part D utilization in the Part D coverage gap or "donut hole" and multiple provisions that could affect the profitability of our drug products. There is continuing development of value-based pricing and reimbursement models. Moreover, on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita Gross Domestic Product-adjusted (GDP-adjusted) price of any non-U.S. member country of the Organization for Economic Co-operation and Development (OECD) with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. Current and future healthcare reform measures may significantly affect our sale of any products, and we continue to face major uncertainty due to the status of major legislative initiatives surrounding healthcare reform.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biologic and chemical substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in other countries that impose similar obligations.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act ("FCPA"), prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business abroad or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

Competition

Companies that are currently engaged in gene therapy or companies not yet focused on developing gene and cell therapies could at any time decide to develop therapies relevant to our business. Many of our competitors, either alone or with their strategic partners, may have substantially greater financial, technical, and human resources than we do and may have significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of product candidates and commercializing those product candidates. Accordingly, our competitors may be more successful than us in obtaining approval for product candidates and achieving widespread market acceptance. Our competitors' product candidates may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates.

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

We anticipate facing intense and increasing competition as new product candidates enter the market and advanced technologies become available. We expect any product candidates that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. 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.

Corporate Information

Our principal executive office is located at 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019. Our telephone number in New York is (646) 813-4701. We also have manufacturing and laboratory facilities and administrative offices in Cleveland, Ohio and office facilities in Madrid, Spain.

We were incorporated in Wyoming in 1974 as Chemex Corporation, and in 1983 we changed our name to Chemex Pharmaceuticals, Inc. We changed our state of incorporation from Wyoming to Delaware on June 30, 1989. In 1996 we merged with Access Pharmaceuticals, Inc., a private Texas corporation, and changed our name to Access Pharmaceuticals, Inc. On October 24, 2014 we changed our name to PlasmaTech Biopharmaceuticals, Inc. On May 15, 2015 we acquired Abeona Therapeutics LLC and on June 19, 2015 we changed our name to Abeona Therapeutics Inc.

Suppliers

Some materials used by us are specialized. We obtain materials from several suppliers based in different countries around the world. If materials are unavailable from one supplier, we generally have alternate suppliers available.

Human Capital Resources

As a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases, we seek to attract, hire, develop and retain qualified and highly skilled personnel with experience in areas such as research and development and manufacturing operations. We compete for such personnel with numerous pharmaceutical and chemical companies, specialized biotechnology firms and universities. We strive to support our employees' well-being through a transparent, inclusive, and collaborative culture and by providing them with the training, support, and resources to help them succeed professionally.

As of March 15, 2021, we had 76 full-time employees. We have never experienced employment-related work stoppages and believe that we maintain good relations with our personnel. In addition, to complement our internal expertise, we have contracts with scientific consultants, contract research organizations and university research laboratories that specialize in various aspects of drug development including clinical development, regulatory affairs, toxicology, process scale-up and preclinical testing.

Web Availability

We make available free of charge through our website, www.abeonatherapeutics.com, our annual reports on Form 10-K and other reports that we file with the Securities and Exchange Commission ("SEC") as well as certain of our corporate governance policies, including the charters for the audit, compensation and nominating and corporate governance committees of the Board of Directors (the "Board") and our code of ethics, corporate governance guidelines and whistleblower policy. We will also provide to any person without charge, upon request, a copy of any of the foregoing materials. Any such request must be made in writing to us at: Abeona Therapeutics Inc. c/o Investor Relations, 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019. The SEC's website, www.sec.gov, contains reports, proxy statements, and other information that we file electronically with the SEC. The content on any website referred to in this Form 10-K is not incorporated by reference in this Form 10-K unless expressly noted.

ITEM 1A. RISK FACTORS

Our business, financial condition, financial results, and future growth prospects are subject to a number of risks and uncertainties, including those set forth below. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, financial results, and future growth prospects. Additional risks and uncertainties that are not currently known to us or that we do not currently believe to be material may also negatively affect our business, financial condition, financial results, and future growth prospects.

RISK FACTOR SUMMARY

Our business is subject to numerous risks and uncertainties, including those described in Item 1A "Risk Factors." These risks include, but are not limited to the following:

- Our gene and cell therapy product candidates are based on proprietary methodologies, which makes it difficult to predict the time and cost of product candidate development and regulatory approval. Additionally, regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future.
- We may encounter substantial delays in our clinical studies or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities. Additionally, we may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.
- We have received and may apply for additional designations such as breakthrough therapy designation, RMAT designation, fast track designation, and rare pediatric disease designation from the FDA intended to facilitate or encourage product candidate development. We may not receive any such designations or be able to maintain them. Moreover, any such designations may not lead to faster development or regulatory review or approval and it does not increase the likelihood that our product candidates will receive marketing approval.
- Certain of our product candidates have received orphan drug designation from the FDA, there is no guarantee that we will be able to maintain this designation, receive this designation for any of our other product candidates, or receive or maintain any corresponding benefits, including periods of exclusivity.
- Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.
- The COVID-19 pandemic and efforts to reduce its spread has affected our operations and significantly impacted worldwide economic conditions, and could continue to have a material effect on our operations, business, and financial condition.
- We could experience production problems in our manufacturing facilities that result in delays in our development or commercialization programs. We might also experience delays in manufacturing if any of our vendors, contract laboratories or suppliers are found to be out of compliance with current Good Manufacturing Practice.
- If we fail to comply with applicable regulations, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the suspension of a clinical trial or commercial sales or the closure of a manufacturing facility.
- We expect to rely on third parties, and these third parties may not perform satisfactorily. Additionally, our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated.
- Our drug candidates are subject to the risks of failure inherent in the development of pharmaceutical products based on new technologies, and our failure to develop safe and commercially viable drugs would severely limit our ability to become profitable or to achieve significant revenues.
- We may be unable to successfully develop, market, or commercialize our products or our product candidates without establishing new relationships and maintaining current relationships and our ability to successfully commercialize, and market our product candidates could be limited if a number of these existing relationships are terminated.

- We may incur substantial product liability expenses due to the use or misuse of our products for which we may be unable to obtain insurance coverage.
- Our ability to successfully develop and commercialize our drug candidates will substantially depend upon the availability of reimbursement funds for the costs of the resulting drugs and related treatments.
- The market may not accept any pharmaceutical products that we develop, and adverse public perception of gene therapy products may negatively affect demand for, or regulatory approval of, our product candidates.
- We may be subject to federal, state, and foreign healthcare laws and regulations, including fraud and abuse laws, false claims laws, health information privacy and security laws and data privacy laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- Our business could suffer if we lose the services of, or fail to attract, key personnel.
- Trends toward managed health care and downward price pressures on medical products and services may limit our ability to profitably sell any drugs that we may develop.
- Our rights to develop and commercialize our product candidates are subject to, in part, the terms and conditions of licenses granted to us by others.
- If we are unable to obtain and maintain patent protection for our product candidates and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours.
- Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation.
- We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.
- We may not be able to protect our intellectual property rights around the world.
- Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court, and intellectual property litigation could cause us to spend substantial resources.
- Third-parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could harm our business.
- We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.
- If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be harmed.
- We have experienced a history of losses; we expect to incur future losses and we may be unable to obtain necessary additional capital to fund operations in the future. We do not have significant operating revenue and may never achieve profitability.
- Failure to achieve and maintain effective internal controls could have a material adverse effect on our business.
- We expect to continue to need to raise additional capital to operate our business, and our failure to obtain funding when needed or on terms that are favorable to us may force us to delay, reduce or eliminate our development programs or aspects thereof.
- The market price of our common stock may be volatile and adversely affected by several factors.
- Raising additional funds by issuing securities or through licensing or lending arrangements or through our at-the-market sale agreement may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights.
- Our quarterly operating results may fluctuate significantly.
- Provisions of our charter documents could discourage an acquisition of our company.
- There can be no assurance that we will be able to comply with continued listing standards of the Nasdaq.
- Ownership of our shares is concentrated in the hands of a few investors, which could limit the ability of our other stockholders to influence the direction of the Company.

Risks related to the discovery and development of our product candidates

Our gene and cell therapy product candidates are based on proprietary methodologies, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Only a few gene therapy products have been approved in the U.S. and the EU.

We have concentrated our therapeutic product research and development efforts on our gene and cell therapy platform, and our future success depends on the successful development of this therapeutic approach. There can be no assurance that any development problems we experience in the future related to our gene and cell therapy platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and commercial-scale manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the FDA, the EMA, and other regulatory agencies 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 ours can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Currently, only a few gene therapy products have been approved in the Western world, including the Spark Therapeutics, Inc. and AveXis, Inc. gene therapy products, which received approval from the FDA in 2018 and 2019, respectively. Additionally, GlaxoSmithKline's Strimvelis® in Europe and Novartis's and Gilead's CAR-T therapies received approval from the FDA in 2017 and 2021. Given the few precedents of approved gene therapy products, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the EU or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, the FDA has established the OTAT within 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.

Regulatory requirements in the United States and in other jurisdictions governing gene therapy products have changed frequently and will continue to change in the future as scientific knowledge is acquired. The FDA and EMA have each expressed interest in further regulating gene therapy. For example, the FDA has established the Office Tissues and Advanced Therapies within 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. Over the last few years, FDA, through CBER, has provided significant guidance regarding the development of gene therapies. Additionally, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some, or all, of our product candidates. These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, 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 studies, limitations, or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

We may encounter substantial delays in our clinical studies, such as clinical holds, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety, purity and potency, and efficacy, of the product candidates in humans. Clinical testing is expensive, time-consuming, and uncertain as to outcome. This is especially true for rare and/or complicated diseases. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing.

The results of preclinical studies, preliminary study results, and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials or the ultimately completed trial. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Preclinical and early clinical studies may also reveal unfavorable product candidate characteristics, including safety concerns. We may also experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or IRBs may not authorize us or our investigators to commence or continue a clinical trial, conduct a clinical trial at a prospective trial site, or amend trial protocols, or regulators or IRBs may require that we modify or amend our clinical trial protocols;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites and our CROs;
- regulators may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing, surveillance, or REMS requirements to maintain regulatory approval;
- flaws in a clinical trial may not become apparent until the trial is well advanced;
- clinical trials of our product candidates may produce negative or inconclusive results, or our studies may fail to reach the necessary level of statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors may fail to comply with regulatory requirements or the clinical trial protocol, or fail to meet their contractual obligations to us in a timely manner, or at all, or we may be required to engage in additional clinical trial site monitoring;
- we, the regulators, or IRBs may require the suspension or termination of clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics (alone or in combination with other products) of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;
- changes in marketing approval and regulatory review policies or changes in or the enactment of additional statutes or regulations;
- the cost of clinical trials of and marketing applications for 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 may be insufficient or inadequate;
- we may decide, or regulators may require us, to conduct or gather, as applicable, additional clinical trials, analyses, reports, data, or preclinical trials, or we may abandon product development programs;
- we may fail to reach an agreement with regulators or IRBs regarding the scope, design, or implementation of our clinical trials. For instance, the FDA or comparable foreign regulatory authorities may require changes to our study design that make further study impractical or not financially prudent;
- we may have delays in adding new investigators or clinical trial sites, or we may experience a withdrawal of clinical trial sites;
- there may be regulatory questions or disagreements regarding interpretations of data and results, or new information may emerge regarding our product candidates;

- we may make changes to our product candidates or their manufacturing process that necessitate additional studies or that result in our product candidates not performing as expected;
- the FDA or comparable foreign regulatory authorities may disagree with our study design, including endpoints, or our interpretation of data from preclinical studies and clinical trials or find that a product candidate's benefits do not outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may not accept data from studies with clinical trial sites in foreign countries;
- the FDA or comparable regulatory authorities may disagree with our intended indications;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or our contract manufacturer's manufacturing facility for clinical and future commercial supplies;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a marketing application, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- regulatory authorities may not accept data from clinical trials conducted in other countries;
- if one of our product candidates does not receive marketing approval in one country, it may impact our ability to receive marketing approval in other countries;
- the FDA or comparable regulatory authorities may take longer than we anticipate to make a decision on our product candidates; and
- we may not be able to demonstrate that a product candidate provides an advantage over current standards of care or current or future competitive therapies in development.

Delays in launching clinical trials resulting from FDA or other regulatory actions, such as a clinical hold letter, would delay the commercialization of our product candidates and our ability to generate revenue, which would have an adverse effect on our business. For example, in September 2019, we received a clinical hold letter in connection with our Phase 3 clinical trial for EB-101 stating that the FDA would not provide approval for us to begin our planned Phase 3 clinical trial for EB-101 until we submitted additional data points on transport stability of EB-101 to clinical sites. Although the FDA removed the clinical hold in December 2019 and provided clearance for us to proceed with our planned Phase 3 clinical trial, we may encounter similar delays in our clinical studies in the future.

Significant delays relating to any preclinical or clinical trials also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do. This may prevent us from receiving marketing approvals and impair our ability to successfully commercialize our product candidates. If any of the foregoing were to occur, our business, financial condition, results of operations, and prospects will be materially harmed.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit eligible patients to participate in testing our product candidates. We have experienced delays in some of our clinical studies due to the ultra-rare nature of the diseases we aim to treat, and we may experience similar delays in the future. If patients are unwilling to participate in our gene and cell therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether.

We may not be able to identify, recruit or enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the study protocol;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical studies;
- efforts to facilitate timely enrollment in clinical studies;
- ability to compensate patients for their time and effort;
- risk that enrolled patients will drop out before completion or not return for post-treatment follow-up;
- inability to obtain or maintain patient informed consents;
- effectiveness of publicity created by clinical trial sites regarding the trial;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Each of the conditions for which we plan to evaluate our current AAV product candidates are rare genetic disorders with limited patient pools from which to draw for clinical studies. Further, because newborn screening is generally not performed for MPS IIIA and MPS IIIB and other diseases we plan to address through gene and cell therapy (e.g., retinal disease), and such diseases can be difficult to diagnose in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our studies. The eligibility criteria of our clinical studies will further limit the pool of available study participants. Additionally, the process of finding and diagnosing patients may prove costly.

We also plan to seek initial marketing approval in the European Union in addition to the U.S. Our ability to successfully initiate, enroll and complete a clinical study in any foreign country is subject to additional risks unique to conducting business in foreign countries, such as different standards for the conduct of clinical studies; different laws, medical standards, and regulatory requirements; and the ability to establish or manage relationships with treatment centers, contract research organizations and physicians.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned our development costs may increase, the time for completion of clinical trials may increase, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which would have an adverse effect on our business.

In addition, enrollment in our Phase 3 VIITAL™ study for EB-101 may encounter some challenges related to identification and enrollment of patients with RDEB. While RDEB is a progressive condition diagnosed in early childhood, not all patients may qualify to participate in our study based on their ability to meet the study inclusion criteria, including criteria related to overall medical condition, type of wounds (recurrent vs. chronic, location, size, etc.), presence of antibodies against collagen VII, or restrictions on the ability to travel to study centers. The process for manufacturing EB-101 requires at least two biopsies from an area of intact skin that must then be shipped to Abeona's manufacturing facility, posing possible risks of transportation, and ultimately viability of the specimens. The clinical trial also requires enrolled patients to travel to the clinical trial site for treatment and follow-up. For individuals with RDEB, traveling can be challenging and pose health risks.

Our products or product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our products or product candidates, including adverse events associated with our product candidates, could interrupt, delay, or halt clinical trials and could result in the denial of regulatory approval or more limited approvals by the FDA, EMA or other regulatory authorities for any or all targeted indications, or the inclusion of unfavorable information in our product labeling, such as limitations on the indicated uses or populations for which the products may be marketed or distributed, a label with significant safety warnings, including boxed warnings, contraindications, and precautions, a label without statements necessary or desirable for successful commercialization, or may result in requirements for costly post-marketing testing and surveillance, or other requirements, including REMS, to monitor the safety or efficacy of the products. These could in turn prevent us from commercializing our products or product candidates and generating revenues from their sale.

In addition, if we or others identify undesirable side effects caused by our product candidates after receipt of marketing approval, the regulatory authorities may require the addition of restrictive labeling statements. Regulatory authorities may withdraw their approval of the product. We also may be required to change the way the product is administered or conduct additional clinical trials. Any of these events could prevent us from achieving or maintaining market acceptance of the affected products or product candidate or could substantially increase the costs and expenses of commercializing the products or product candidate, which in turn could delay or prevent us from generating significant revenues from its sale or adversely affect our reputation.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a narrower indication than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies 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 advisory group or authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based on additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies, and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications, populations, or uses than requested or may grant approval subject to the performance of post-marketing studies, surveillance, or other requirements. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates, or may require significant safety warnings, including black box warnings, contraindications, and precautions. For example, the development of our product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

We have received and may apply for additional designations intended to facilitate or encourage product candidate development. We may not receive any such designations or be able to maintain them. Moreover, any such designations may not lead to faster development or regulatory review or approval and it does not increase the likelihood that our product candidates will receive marketing approval.

Our product candidates have received regulatory designations including breakthrough therapy designation, RMAT designation, fast track designation, and rare pediatric disease designation from the FDA. In the future and as appropriate, we may seek additional product designations. Receipt of such a designation is within the discretion of the FDA. Even if we believe one of our product candidates meets the criteria for a designation, the FDA may disagree. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate marketing approval by the FDA. In addition, the FDA may later decide that the product candidates no longer meet the designation conditions, in which case any granted designations may be revoked. Finally, specifically with respect our rare pediatric disease designations, if we are not able to obtain FDA approval of our designated product candidates before the statute sunsets, we would not be eligible to receive priority review vouchers.

Certain of our product candidates have received orphan drug designation from the FDA, there is no guarantee that we will be able to maintain this designation, receive this designation for any of our other product candidates, or receive or maintain any corresponding benefits, including periods of exclusivity.

While orphan drug designation provides certain advantages, it neither shortens the development time or regulatory review time of a product candidate nor gives the product candidate any advantage in the regulatory review or approval process. Generally, if a product candidate with orphan drug designation subsequently receives marketing approval before another product considered by the FDA or comparable foreign regulatory authorities to be the same, for the same orphan indication, the product is entitled to a period of marketing exclusivity, which precludes the FDA or comparable foreign regulatory authorities from approving another marketing application for the same drug or biologic for the same indication for seven years. We may not be able to obtain any future orphan drug designations that we apply for, orphan drug designations do not guarantee that we will be able to successfully develop our product candidates, and there is no guarantee that we will be able to maintain any orphan drug designations that we receive. For instance, orphan drug designation may be revoked if the FDA finds that the request for designation contained an untrue statement of material fact or omitted material information, or if the FDA finds that the product candidate was not eligible for designation at the time of the submission of the request. Moreover, we may ultimately not receive any period of regulatory exclusivity if our product candidates are approved. For instance, we may not receive orphan product regulatory exclusivity if the indication for which we receive FDA approval is broader than the designation. Orphan exclusivity may also be lost for the same reasons that the designation may be lost. Orphan exclusivity may further be lost if we are unable to assure a sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan exclusivity for any of our current or future product candidates, that exclusivity may not effectively protect the product from competition as different products can be approved for the same condition or products that are the same as ours can be approved for different conditions. Even after an orphan product is approved, the FDA or comparable foreign regulatory authorities can also subsequently approve a product containing the same principal molecular features for the same condition if the FDA concludes that the later product is clinically superior. The FDA may further grant orphan drug designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA or comparable foreign regulatory authority approval for such product before we do, we would be prevented from launching our product for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority. FDA's thinking around sameness with respect to gene therapies, and thus the circumstances when clinical superiority would need to be shown, is evolving. While the agency has issued a guidance on the topic, certain decisions may need to be made on a case by case basis, given the novelty of the technology. Moreover, third-party payors may reimburse for products off-label even if not indicated for the orphan condition.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

Even if we obtain regulatory approval in a jurisdiction, regulatory authorities may still impose significant restrictions on the indicated uses or marketing of our product candidates or impose ongoing requirements for potentially costly post-approval studies, post-market surveillance or patient or drug restrictions. Moreover, the FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval, including gene therapy specific requirements for long term follow up. Additionally, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP and adherence to commitments made in the BLA. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or that the product is less effective than previously thought, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates or during product development, or if we later discovery previously unknown safety, efficacy, or manufacturing issues, the following may result:

- restrictions on manufacturing, distribution, marketing, or labeling of such products, including restrictions on the indication or approved patient population, and required additional warnings, such as black box warnings, contraindications, and precautions;
- requirements to conduct post-marketing studies or clinical trials, or to institute risk mitigation strategies, such as REMS;
- issuance of corrective information;
- the product may become less competitive, we may face reputational harm, or we may face liability for any harm caused to patients or subjects;
- modifications on the way the product is administered;
- modifications on promotional pieces;
- issuance of warning, untitled, or cyber letters asserting that we are in violation of the law, or of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- injunction or imposition civil or criminal penalties or monetary fines, restitution, or disgorgement of profits or revenues;
- suspension or withdrawal of regulatory approval;
- suspension or termination of any ongoing clinical studies;
- refusal to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us;
- seizure, detention, or recall of product;
- refusal to permit the import or export of our products; or
- refusal to allow us to enter into supply contracts, including government contracts, exclusion from federal healthcare programs, FDA debarment, consent decrees, or corporate integrity agreements.

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 generate revenues.

The FDA's policies may change, and additional government regulations may be enacted, that could prevent, limit or delay regulatory approval of our product candidates, that could limit the marketability of our product candidates, or that could impose additional regulatory obligations on us. For example, the change in administration in the U.S. may result in new, revised, postponed or frozen regulatory requirements and associated compliance obligations. Changes in medical practice and standard of care may also impact the marketability of our product candidates. If we are slow or unable to adapt to changes in existing requirements, standards of care, or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and be subject to regulatory enforcement action.

Should any of the above actions take place, they could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

The COVID-19 pandemic and efforts to reduce its spread have affected our operations and significantly impacted worldwide economic conditions, and could continue to have a material effect on our operations, business and financial condition.

To date, the COVID-19 pandemic has resulted in intermittent shutdowns of non-essential businesses throughout the world. The impact of the COVID-19 pandemic has also resulted in social, economic, and labor instability in the countries in which we, or the third parties with whom we engage, operate. Public health officials have recommended precautions to mitigate the spread of the coronavirus, including prohibitions on congregating in heavily populated areas and shelter-in-place orders. As a result, our operations at our Cleveland manufacturing facility were significantly scaled back during a portion of 2020 to ensure that our employees and those around them had the best chance to remain safe and to accommodate reduced manufacturing and clinical development activities.

The COVID-19 pandemic has substantially burdened healthcare systems worldwide, delaying enrollment in and progression of our clinical trials. Required inspections and reviews by regulatory agencies have also been delayed due to the focus of resources on COVID-19, as well as travel and other restrictions. For example, our Phase 3 VIITAL™ clinical trial was temporarily paused in March 2020 due to the COVID-19 pandemic and the restrictions established by our clinical trial site at Stanford University in Palo Alto, California, but resumed in June 2020. Significant delays in the timing of our clinical trials and in regulatory reviews could adversely affect our ability to commercialize our product candidates.

Although we remain committed to advancing our clinical programs, we recognize some delays are inevitable in light of the closure of non-essential businesses, stay at home orders, and economic impacts related to the COVID-19 pandemic, especially as healthcare resources have been justly redirected to those who need them most. Many of the third parties with whom we engage, including suppliers, clinical trial sites, regulators and other third parties with whom we conduct business, are also experiencing shutdowns or other business disruptions. Despite our current clinical trial sites gradually resuming activities on site and us having resumed our EB-101 manufacturing activities in the later part of 2020, we may continue to experience disruptions that could severely impact our business, supply chain, manufacturing operations, clinical trials, and pre-clinical studies, including:

- continued interruption of key clinical trial activities, including continued limitations on travel imposed or recommended by federal or state governments, employers, and others;
- the need to postpone, modify, suspend, or terminate clinical trials;
- patients may withdraw from clinical trials;
- we may experience study or manufacturing deviations or noncompliance, requiring that we consult with regulatory authorities, and IRBs, and which may compromise the ultimate study results or quality of the manufactured products;
- continued delays or inability to obtain raw materials, ingredients, or other necessary supplies, including if third party suppliers need to prioritize other products or customers over us, including under the Defense Production Act;
- continued delays or difficulties in enrolling patients in our clinical trials;
- continued delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or difficulties in manufacturing clinical drug material;
- continued diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; and
- continued limitations in employee resources that would otherwise be focused on the conduct of our manufacturing operations, clinical trials, and preclinical studies, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

The ultimate impact of the COVID-19 pandemic remains uncertain and subject to change. Due to the potential impact of the COVID-19 outbreak on clinical trials, drug development, and manufacturing, FDA issued guidance concerning how sponsors and investigators may address these challenges, as well as guidance specific to gene therapies and comparable foreign regulatory authorities have done likewise. This guidance recommended that gene therapy manufacturers perform a risk assessment to identify, evaluate, and mitigate factors that may allow for the transmission of the SARS-CoV-2 virus. FDA specifically recommended that manufacturers consider areas, such as donor assessments, cellular and tissue source materials, manufacturing processes, manufacturing facility controls, product and material testing, and the number of individuals who may receive the product. Per the guidance, risk assessment and mitigation strategies should be submitted to FDA.

The COVID-19 pandemic may also result in changes in laws and regulations. For example, in March 2020, the U.S. Congress passed the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, which includes various provisions regarding FDA drug shortage reporting requirements, as well as provisions regarding supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy and domestic manufacturing. This and any future changes in law may require that we change our internal processes and procedures to ensure continued compliance. We do not yet know the full extent of potential delays or impacts on our business, operations, or financial condition, or on healthcare systems or the global economy as a whole. However, these effects could have a material impact on our ability to access the capital markets as needed and on our operations and business, and those of the third parties on which we rely.

Risks related to manufacturing

We could experience production problems in our manufacturing facilities that result in delays in our development or commercialization programs or otherwise adversely affect our business.

We are susceptible to production interruptions that may impede our ability to manufacture gene and cell therapy products and produce an adequate product supply to support clinical trials and potentially future commercialization. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, public health emergencies such as the coronavirus, disruption in utility services, human error, or disruptions in the operations of our suppliers. Our products and product candidates are biologic drugs requiring processing steps that are more complex than those required for most chemical pharmaceuticals. We characterize our processes and products, and perform testing to ensure the safety, quality and efficacy of each product produced. While we take significant measures to fully understand and characterize each product, the steps we take may not be sufficient to ensure that a given lot will perform in the intended manner.

There are several risks specific to the manufacturing process for EB-101 which require close attention. As an autologous product there are challenges associated with viability of biopsies as an incoming material. Due to variables such as the fragility of RDEB skin and site of the biopsy, initiation of autologous keratinocyte growth and expansion can be challenging or may be extended beyond the scheduled timing. Another concern during manufacturing is the slowing of cell proliferation, resulting in extended manufacturing time. If pre-release criteria are not met, the production process must be stopped and a new biopsy must be obtained. If release criteria are out of range, epidermal sheets must be discarded and the manufacturing process must be repeated.

We currently do not have a backup manufacturer to supply clinical trial material for EB-101. An alternative manufacturer would need to be qualified, through regulatory filings, which could result in delays to our clinical trial timeline. The regulatory authorities also may require additional clinical trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

Accordingly, we employ multiple steps to control our manufacturing process to assure that the products or product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, including even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, EU or other applicable standards or specifications with consistent and acceptable production yields and costs. In addition, FDA, EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls for approved and marketed products.

Lot failures or product recalls could cause us to delay product launches or clinical trials, 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 specialist scientific, quality control and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our manufacturing process or facilities 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 our manufacturing process including in internal and external facilities providing supply necessary for manufacturing or challenges with procuring supplies, such as due to global trade policies, also could restrict our ability to meet clinical trial supply demand, and eventually market demand for any product candidates for which we may receive marketing approval. Disruptions in our manufacturing process may delay or disrupt our commercialization efforts.

If we or any of our vendors, contract laboratories or suppliers are found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we implement corrective actions or work with these third parties to remedy the violation or while we work to identify suitable replacement vendors, contract laboratories or suppliers.

To obtain regulatory approval for commercial manufacturing, we will need to continue to ensure that all of our processes, methods and equipment are compliant with cGMP and perform extensive audits of vendors, contract laboratories and suppliers. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. Complying with cGMP requires us to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

We may rely on third parties to conduct aspects of our product manufacturing, and these third parties may not perform satisfactorily. We may rely on third parties to produce certain materials for our product candidates and, therefore, we can control only certain aspects of their activities.

We and our third party suppliers, laboratories, and manufacturers may be unable to comply with our specifications, cGMP requirements and with other FDA, state, and foreign regulatory requirements. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing. If we or our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. Any such deviations may also require remedial measures that may be costly and/or time-consuming for us or a third party to implement and may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon or by us or third parties with whom we contract could materially harm our business. Any delays in obtaining products or product candidates that comply with the applicable regulatory requirements may result in delays to clinical trials, product approvals, and commercialization. It may also require that we conduct additional studies.

We have manufacturing agreements with third parties that provide for, among other things, production of product candidates for our current and future early stage clinical trials. Under certain circumstances, the other party is entitled to terminate its arrangement with us. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on third parties for certain manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. If a third party does not successfully carry out its contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, or if there are disagreements between us and any such third party, we will not be able to complete, or may be delayed in completing, the preclinical studies required to support future IND submissions and the clinical trials required for approval of our product candidates. In such instances, we may need to enter into an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, which would cause additional delay or increased expense prior to the approval of our product candidates and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, if the FDA or a comparable foreign regulatory authority does not approve our or a third party's facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain and maintain regulatory approval for or market our product candidates, if approved. Any new manufacturers would need to either obtain or develop the necessary manufacturing know-how, and obtain the necessary equipment and materials, which may take substantial time and investment. We must also receive FDA approval for the use of any new manufacturers for commercial supply. We may not succeed in our efforts to establish manufacturing relationships or other alternative arrangements for any of our product candidates, components, and programs. For example, our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so.

The manufacture of biologic products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of therapeutics often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, and compliance with strictly enforced federal, state, and foreign regulations. If we or our manufacturers were to encounter any of these difficulties and were unable to perform as agreed, our ability to provide product candidates to patients in our clinical trials and for commercial use, if approved, would be jeopardized.

Our reliance on these third parties entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;
- reduced control over the protection of our trade secrets and know-how from misappropriation or inadvertent disclosure;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reliance on the third party for regulatory compliance and quality assurance;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future product candidates. Some of these events could be the basis for FDA action or action of equivalent competent authorities in foreign jurisdictions, including injunction, recall, seizure or total or partial suspension of product manufacture. Failure to comply with ongoing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

If any inspection or audit by regulatory authorities identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility.

Regulatory authorities may inspect or audit the manufacturing facilities for our products and product candidates at any time. Any such remedial measures imposed upon us could materially harm our business, financial condition, results of operations and prospects. If we fail to comply with applicable cGMP regulations, FDA and foreign regulatory authorities could impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be materially harmed. Additionally, if supply from our facility is interrupted, there could be a significant disruption in commercial supply of any of our product candidates for which we obtain marketing approval, and in clinical supply for our product candidates.

If we, our collaborators, or any third-party manufacturers 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 harm our business.

We, our collaborators, and any third-party manufacturers we engage are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic materials. Our operations also produce hazardous waste products. 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. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain general liability insurance and workers' compensation insurance for certain costs and expenses that we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic or hazardous materials.

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

Risks related to our reliance on third-parties

We expect to rely on third parties to conduct some or all aspects of our viral vector production, drug product manufacturing, research and preclinical, and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our viral vector production, drug product manufacturing and distribution, research and preclinical, and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these matters. In some cases, these third parties are academic, research or similar institutions that may not apply the same quality control protocols utilized in certain commercial settings.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we remain responsible for ensuring that each of our IND-enabling studies and clinical studies are conducted in accordance with the study plan and protocols, and that our viral vectors and drug products are manufactured in accordance with GMP as applied in the relevant jurisdictions. We must also ensure that our preclinical trials are conducted in accordance with GLPs, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with GCPs 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. Regulatory authorities enforce these requirements through periodic inspections. If we or any of our third-party service providers fail to comply with applicable regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials or manufacturing development may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional studies and manufacturing development. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, or manufacture our viral vectors and drug products in accordance with GMP, or if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies and manufacturing process validation activities required to support future IND, MAA and BLA submissions and approval of our product candidates.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Any of these events could lead to clinical study delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to manufacture our vectors and our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our gene and cell therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees, and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks associated with commercializing our product candidates

Our drug candidates are subject to the risks of failure inherent in the development of pharmaceutical products based on new technologies, and our failure to develop safe and commercially viable drugs would severely limit our ability to become profitable or to achieve significant revenues.

We may be unable to successfully commercialize our product candidates if some or all of our product candidates are found to be unsafe or ineffective or otherwise fail to meet applicable regulatory standards or receive necessary regulatory clearances. Additionally, our product candidates may be deemed too difficult to develop into commercially viable drugs. We may encounter difficulty in manufacturing or marketing our product candidates on a large scale, and proprietary rights of third parties may preclude us from marketing our drug candidates. Moreover, competitors may be able to market superior or equivalent drugs successfully. Failure to successfully commercialize our product candidates would have a material adverse effect on our business.

We may be unable to successfully develop, market, or commercialize our products or our product candidates without establishing new relationships and maintaining current relationships and our ability to successfully commercialize, and market our product candidates could be limited if a number of these existing relationships are terminated.

Our strategy for the research, development and commercialization of our potential pharmaceutical products may require us to enter into various arrangements with corporate and academic collaborators, licensors, licensees and others, in addition to our existing relationships with other parties. Specifically, we may seek to joint venture, sublicense or enter into other marketing arrangements with parties that have an established marketing capability, or we may choose to pursue the commercialization of such products on our own. We may, however, be unable to establish such additional collaborative arrangements, license agreements, or marketing agreements as we may deem necessary to develop, commercialize and market our potential pharmaceutical products on acceptable terms. Furthermore, we maintain and establish arrangements or relationships with third parties, our business may depend upon the successful performance by these third parties of their responsibilities under those arrangements and relationships. If we are unwilling or unable to perform our obligations under any license or collaboration arrangement, a third party may have the right to terminate such arrangement with us.

We are subject to extensive governmental regulation, which increases our cost of doing business and may affect our ability to commercialize any new products that we may develop.

The FDA and comparable agencies in foreign countries impose substantial requirements upon the introduction of pharmaceutical products through lengthy and detailed laboratory, preclinical and clinical testing procedures and other costly and time-consuming procedures to establish safety and efficacy. All of our drugs and drug candidates require receipt and maintenance of governmental approvals for commercialization. Preclinical and clinical trials and manufacturing of our drug candidates will be subject to the rigorous testing and approval processes of the FDA and corresponding foreign regulatory authorities. Satisfaction of these requirements typically takes a significant number of years and can vary substantially based upon the type, complexity, and novelty of the product.

Due to the time-consuming and uncertain nature of the drug candidate development process and the governmental approval process described above, we cannot be certain when we, independently or with our collaborative partners, might submit a BLA for FDA or other regulatory review. Further, our ability to commence and/or complete development projects will be subject to our ability to raise enough funds to pay for the development costs of these projects. Government regulation also affects the manufacturing and marketing of pharmaceutical products. Government regulations may delay marketing of our potential drugs for a considerable or indefinite period of time, impose costly procedural requirements upon our activities and furnish a competitive advantage to larger companies or companies more experienced in regulatory affairs. Delays in obtaining governmental regulatory approval could adversely affect our marketing as well as our ability to generate significant revenues from commercial sales.

Our drug candidates may not receive FDA or other regulatory approvals on a timely basis or at all. Moreover, if regulatory approval of a drug candidate is granted, such approval may impose limitations on the indicated use for which such drug may be marketed. Even if we obtain initial regulatory approvals for our drug candidates, our drugs and our manufacturing facilities would be subject to continual review and periodic inspection, and later discovery of previously unknown problems with a drug, manufacturer or facility may result in restrictions on the marketing or manufacture of such drug, including withdrawal of the drug from the market. The FDA and other regulatory authorities stringently apply regulatory standards and failure to comply with regulatory standards can, among other things, result in fines, denial or withdrawal of regulatory approvals, product recalls or seizures, operating restrictions, and criminal prosecution.

We may incur substantial product liability expenses due to the use or misuse of our products for which we may be unable to obtain insurance coverage.

Our business exposes us to potential liability risks that are inherent in the testing, manufacturing, and marketing of pharmaceutical products. These risks will expand with respect to our drug candidates, if any, that receive regulatory approval for commercial sale and we may face substantial liability for damages in the event of adverse side effects, including injury or death, or product defects identified with any of our products that are used in clinical tests or marketed to the public. Product liability actions can also have regulatory consequences, including the withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs, and the initiation of investigations, and enforcement actions by regulators, product recalls, withdrawals, revocation of approvals, or labeling, marketing, or promotional restrictions.

Product liability insurance for the biotechnology industry is generally expensive, if available at all, and as a result, we may be unable to obtain insurance coverage at acceptable costs or in a sufficient amount in the future, if at all. We may be unable to satisfy any claims for which we may be held liable as a result of the use or misuse of products which we developed, manufactured, or sold and any such product liability claim could adversely affect our business, operating results, or financial condition.

Intense competition may limit our ability to successfully develop and market commercial products.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Our competitors in the U.S. and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. Many of our competitors have and employ greater financial and other resources, including larger research and development, marketing, and manufacturing organizations. As a result, our competitors may successfully develop technologies and drugs that are more effective or less costly than any that we are developing, which could render our technology and future products obsolete and noncompetitive.

In addition, some of our competitors have greater experience than we do in conducting preclinical and clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals for drug candidates more rapidly than we can. Companies that complete clinical trials, obtain required regulatory agency approvals, and commence commercial sale of their drugs before their competitors may achieve a significant competitive advantage. Drugs resulting from our research and development efforts or from our joint efforts with collaborative partners therefore may not be commercially competitive with our competitors' existing products or products under development.

Our products and product candidates may face competition sooner than anticipated.

Our products and product candidates may face competition from other products that are the same as or similar to ours. If the FDA or comparable foreign regulatory authorities approve biosimilar versions of our products or product candidates, or such authorities do not grant our products appropriate or anticipated periods of regulatory exclusivity, the sales of our products could be adversely affected. Moreover, even if we receive periods of regulatory exclusivity, that exclusivity may not adequately protect us from biosimilar or other product competition. There may also be changes in regulatory exclusivity policies. For example, there have been efforts to decrease the biologic period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity. If another company pursues approval of a product that is biosimilar to any biologic product for which we receive FDA approval, we may need to pursue costly and time consuming patent infringement actions, which may include certain statutorily specified regulatory steps before an infringement action may be brought. Biosimilar applicants may also be able to bring an action for declaratory judgment concerning our patents, requiring that we spend time and money defending the action.

Our ability to successfully develop and commercialize our drug candidates will substantially depend upon the availability of reimbursement funds for the costs of the resulting drugs and related treatments.

Market acceptance and sales of our product candidates may depend on coverage and reimbursement policies and health care reform measures. Decisions about formulary coverage as well as levels at which government authorities and third-party payers, such as private health insurers and health maintenance organizations, reimburse patients for the price they pay for our products as well as levels at which these payors pay directly for our products, where applicable, could affect whether we are able to commercialize these products. We cannot be sure that reimbursement will be available for any of these products. Also, we cannot be sure that coverage or reimbursement amounts will not reduce the demand for, or the price of, our products. We have not commenced efforts to have our product candidates reimbursed by government or third-party payors. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to commercialize our products. In recent years, officials have made numerous proposals to change the health care system in the U.S. These proposals include measures that would limit or prohibit payments for certain medical treatments or subject the pricing of drugs to government control. In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. If our products are or become subject to government regulation that limits or prohibits payment for our products, or that subjects the price of our products to governmental control, we may not be able to generate revenue, attain profitability or commercialize our products.

As a result of legislative proposals and the trend towards managed health care in the U.S., third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also impose strict prior authorization requirements and/or refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly-approved drugs, which in turn will put pressure on the pricing of drugs.

The market may not accept any pharmaceutical products that we develop, thereby materially impairing our ability to generate revenue from such products.

The products that we are attempting to develop may compete with a number of well-established drugs manufactured and marketed by major pharmaceutical companies. The degree of market acceptance of any drugs developed by us will depend on a number of factors, including the establishment and demonstration of the clinical efficacy and safety of our drug candidates, the potential advantage of our drug candidates over existing therapies and the reimbursement policies of government and third-party payers. Physicians, patients, or the medical community in general may not accept or use any drugs that we may develop independently or with our collaborative partners and if they do not, our business could suffer.

Adverse public perception of gene therapy products may negatively affect demand for, or regulatory approval of, our product candidates.

Our product candidates involve altering genes, and the clinical and commercial success of our product candidates will depend in part on public acceptance of the use of gene altering therapies for the treatment of genetic diseases. Public attitude may be influenced by claims that gene therapy is unsafe, unethical, or immoral, and, as a result, our product candidates may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene therapy products, including any of our product candidates, and could cause a decrease in the demand for any products we may develop. Adverse public opinion also may adversely affect our ability to enroll patients in clinical trials.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

Any government-adopted reform measures could adversely affect the pricing of healthcare products and services in the U.S. or internationally and the amount of reimbursement available from governmental agencies or other third-party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect our ability to set prices for our products which we believe are fair, restrict coverage and reimbursement, or require payment of increased rebates and our ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations, and decisions, that relate to healthcare availability, methods of delivery or payment for products and services, or sales, marketing, or pricing, may limit our potential revenue, and we may need to revise our research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons including new healthcare legislation or regulation and fiscal challenges faced by government health administration authorities. Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad.

We may be subject, directly or indirectly, to federal, state, and foreign healthcare laws and regulations, including fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our prescribers, customers, and purchasers, subject to various federal and state laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims act, the civil monetary penalties statute, HIPAA, and the Physician Payments Sunshine Act and regulations. These laws are further described in the U.S. Biologic Products Development Process section of this annual report. These laws will impact, among other things, our proposed sales, marketing, and educational programs. In addition, we may be subject to data privacy laws by both the federal government and the states in which we conduct our business. Failure to comply with these laws could result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs, debarment from government contracting or refusal of orders under existing contracts, corporate integrity agreements or consent decrees, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly. Comparable laws and regulations apply internationally.

We are subject to extensive laws and regulations related to data privacy, and our failure to comply with these laws and regulations could harm our business.

Numerous foreign, federal, and state laws and regulations govern collection, dissemination, use and confidentiality of personally identifiable health information, including state privacy and confidentiality laws (including state laws requiring disclosure of breaches), HIPAA and the European Union's General Data Protection Regulation ("GDPR"). These laws and regulations are increasing in complexity and number and may change frequently and sometimes conflict.

HIPAA establishes a set of national privacy and security standards for the protection of individually identifiable health information, including protected health information ("PHI"), by health plans, certain healthcare clearinghouses and healthcare providers that submit certain covered transactions electronically, or covered entities, and their "business associates," which are persons or entities that perform certain services for, or on behalf of, a covered entity that involve creating, receiving, maintaining or transmitting PHI. While we are not currently a covered entity or business associate under HIPAA, we may receive identifiable information from these entities. Failure to protect this information properly could subject us to HIPAA's criminal penalties, which may include fines up to $250,000 per violation and/or imprisonment.

GDPR imposes numerous requirements on entities that process personal data in the context of an establishment in the European Economic Area ("EEA") or that process the personal data of data subjects who are located in the EEA. These requirements include, for example, establishing a basis for processing, providing notice to data subjects, developing procedures to vindicate expanded data subject rights, implementing appropriate technical and organizational measures to safeguard personal data, and complying with restrictions on the cross-border transfer of personal data from the EEA to countries that the European Union does not consider to have in place adequate data protection legislation, such as the United States. GDPR additionally establishes heightened obligations for entities that process "special categories" of personal data, such as health data. Nearly all clinical trials involve the processing of these "special categories" of personal data, and thus processing of personal data collected during the course of clinical trials is subject to heightened protections under GDPR.

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

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

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, as well as personally identifiable information of clinical trial participants and employees. Similarly, our business partners and third-party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance, or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost, or stolen. 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 or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed.

Our business could suffer if we lose the services of, or fail to attract, key personnel.

We depend highly upon the efforts of our senior management. The loss of the services of these individuals could delay or prevent the achievement of our research, development, marketing, or product commercialization objectives. We do not have employment contracts with our other key personnel. We do not maintain any "key-man" insurance policies on any of our key employees and we do not intend to obtain such insurance. In addition, due to the specialized scientific nature of our business, we are highly dependent upon our ability to attract and retain qualified scientific and technical personnel and consultants. There is intense competition among major pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions for qualified personnel in the areas of our activities and we may be unsuccessful in attracting and retaining these personnel.

We have experienced turnover in our senior management team, and the loss of one or more of our executive officers or key employees or an inability to attract and retain highly skilled employees could adversely affect our business.

Our success depends largely upon the continued services of our key executive officers. We have in the past and may in the future experience changes in our executive management team resulting from the departure of executives or subsequent hiring of new executives, which may be disruptive to our business. To continue to develop our pipeline and execute our strategy, we also must attract and retain highly skilled personnel in our industry.

Trends toward managed health care, health technology assessment, and downward price pressures on medical products and services may limit our ability to profitably sell any drugs that we may develop.

Lower prices for pharmaceutical products or reduced profitability may result from:

- third-party-payers' increasing challenges to the prices charged for medical products and services, including by limiting coverage and reimbursement and requiring payment of increased manufacturer rebates;
- the trend toward managed health care in the U.S. and the concurrent growth of HMOs and similar organizations that can control or significantly influence the purchase of healthcare services and products; and
- state, federal, and foreign legislative proposals to control drug prices, reform healthcare or reduce government insurance programs.

The cost containment measures that healthcare providers are instituting, including practice protocols and guidelines and clinical pathways, and the effect of any healthcare reform, could limit our ability to profitably sell any drugs that we may successfully develop. Moreover, any future legislation or regulation, if any, relating to the healthcare industry or third-party coverage and reimbursement, may cause our business to suffer.

Risks related to our intellectual property

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

We rely upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. These licenses may also require us to grant back certain rights to licensors and to pay certain amounts relating to sublicensing patent and other rights under the agreement.

In some circumstances, particularly in-licenses with academic institutions, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering in-licensed technologies. Therefore, in those cases we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In certain circumstances, we have or may license technology from third parties on a non-exclusive basis. In such instances, other licensees may have the right to enforce our licensed patents in their respective fields, without our oversight or control. Those other licensees may choose to enforce our licensed patents in a way that harms our interest, for example, by advocating for claim interpretations or agreeing on invalidity positions that conflict with our positions or our interest. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future.

Further, in many of our license agreements we are responsible for bringing any actions against any third party for infringing the patents we have licensed. Certain of our license agreements also require us to meet development milestones to maintain the license, including establishing a set timeline for developing and commercializing products and minimum yearly diligence obligations in developing and commercializing the product. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe intellectual property rights of the licensor that are not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the inventorship or ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If any dispute over in-licensed intellectual property prevents or impairs our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

If we fail to comply with our obligations under these license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop, manufacture, or market products covered by the license or may face other penalties under the agreements. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. It is possible that such termination may occur even if we believe that we have complied with our obligations under a license agreement, if a dispute arises between us and a licensor. Our license agreement with REGENXBIO had granted us an exclusive worldwide license (subject to certain non-exclusive rights previously granted for MPS IIIA), with rights to sublicense, to use REGENXBIO's NAV AAV9 capsid in gene therapies for treating MPS IIIA, MPS IIIB, CLN1 Disease, and CLN3 Disease. On May 2, 2020, REGENXBIO terminated the license agreement. We filed an arbitration claim against REGENXBIO relating to $28 million plus interest that REGENXBIO argues remains due following the agreement's termination. An arbitration hearing before a tribunal of three arbitrators of the American Arbitration Association ("AAA") was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021. We may not prevail in the arbitration proceeding. Even if we do prevail, it is possible that REGENXBIO may in the future assert that our proposed products infringe one or more of REGENXBIO's AAV9 patent claims, and we still may ultimately need a license to use the AAV9 capsid in our proposed MPS IIIA, MPS IIIB, and CLN3 products, if such a product is commercialized before the expiration of one or more REGENXBIO patent claims that cover our commercial product. Absent such a license, if we are found to infringe a REGENXBIO AAV9 patent claim before the expiration of a relevant REGENXBIO patent, it is possible that a court may enjoin the sale of one or more of our proposed AAV9-based products, order us to pay a less favorable royalty rate to REGENXBIO than the royalty rate in the original license agreement, or order us to pay other damages.

Furthermore, to the extent that the research resulting in certain of our licensed patent rights and technology was funded by the U.S. government, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive, royalty-free license authorizing the U.S. government, or a third party on its behalf, to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The U.S. government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government, or a third party on its behalf, of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

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

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

The patent prosecution process is expensive, time-consuming and complex, and we may not have and may not in the future be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. For example, in some cases, the work of certain academic researchers in the gene therapy field has entered the public domain, which may compromise our ability to obtain patent protection for certain inventions related to or building upon such prior work. Consequently, we will not be able to obtain any such patents to prevent others from using our technology for, and developing and marketing competing products to treat, these indications. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensors' patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our and our licensors' patent protection.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all.

Therefore, we cannot be certain that we were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Databases for patents and publications, and methods for searching them, are inherently limited, so it is not practical to review and know the full scope of all issued and pending patent applications. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensed patent rights are uncertain.

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

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. 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.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to develop our program.

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

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

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

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 could be less extensive than in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from 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 enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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 products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, an April 2014 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could harm our business.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. Some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, collaborators, contractors, and other third-parties. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Third-parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may become party to, or threatened with, infringement litigation claims regarding our product candidates and technology, including claims from competitors or from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect. Moreover, we may become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference or derivation proceedings, post grant review and *inter partes* review before the USPTO or foreign patent offices. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could adversely affect our ability to commercialize our product candidates or any other of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a statutory presumption of validity. As this burden is a high one requiring us to prove by clear and convincing evidence 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. Similar challenges exist in other jurisdictions. If we are found to infringe a third-party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third-party to continue developing, manufacturing, and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals, and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, reputation, financial condition, results of operations and prospects.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Competitors may infringe our intellectual property rights or the intellectual property rights of our licensing partners, or we may be required to defend against claims of infringement. To counter infringement or unauthorized use claims or to defend against claims of infringement can be expensive and time consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to 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 adversely affect our ability to compete in the marketplace.

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

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

If we fail in prosecuting or 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 prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Our success depends heavily on intellectual property, especially on patents. Obtaining and enforcing patents in the gene therapy industry involves both technological and legal complexity. Therefore, obtaining and enforcing patents is costly, time-consuming, and inherently uncertain.

As of 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications claiming the same invention are filed by different parties. A third party that files a patent application in the USPTO before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. The change to "first-to-file" from "first-to-invent" is one of the changes to the patent laws of the U.S. resulting from the Leahy-Smith America Invents Act (the "AIA"). Among some of the other significant changes to the patent laws are changes that limit where a patentee may file a patent infringement suit and provide opportunities for third parties to challenge any issued patent in the USPTO via procedures including post-grant and *inter partes* review. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than that used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any issued patents, all of which could harm our business and financial condition.

We also may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in other contested proceedings such as opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be 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 patent term extension ("PTE") under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a PTE of up to five years as compensation for patent term lost during the FDA regulatory review process. PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended per FDA-approved product, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Further, certain of our licenses currently or in the future may not provide us with the right to control decisions of the licensor or its other licensees with respect to PTE under the Hatch-Waxman Act. Thus, if one of our important licensed patents is eligible for PTE, and it covers a product of another licensee in addition to our own product candidate, we may not be able to obtain that extension if the other licensee seeks and obtains that extension first. Moreover, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements, or the applicable time-period or the scope of patent protection afforded during any such extension could be less than we request. If we are unable to obtain PTE or the duration of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be materially reduced.

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 such rights may not adequately protect our business or permit us to maintain our competitive advantage. For example:

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

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

Risks relating to our financial condition and capital requirements

We have experienced a history of losses; we expect to incur future losses and we may be unable to obtain necessary additional capital to fund operations in the future.

We have recorded minimal revenue to date and have incurred an accumulated deficit of approximately $570.7 million through December 31, 2020. The net loss for the year ended December 31, 2020 was $84.2 million, including a $32.9 million licensed technology impairment charge. Our losses have resulted principally from costs incurred in research and development activities related to our efforts to develop clinical drug candidates, from losses due to derivatives and from the associated administrative costs.

We require substantial capital for our development programs and operating expenses, to pursue regulatory clearances and to prosecute and defend our intellectual property rights. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- further develop the manufacturing process for our vectors or our product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under any license agreements;
- maintain, protect and expand our intellectual property portfolio;

- establish a sales, marketing and distribution infrastructure in the United States and Europe to commercialize any products for which we may obtain marketing approval;
- attract and retain skilled personnel;
- build additional infrastructure to support our operations as a larger public company and our product development and planned future commercialization efforts, including manufacturing capacity; and
- experience any delays or encounter issues with any of the above.

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. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

As of December 31, 2020, our cash, cash equivalents and short-term investments were $95.0 million. We expect that our existing cash and cash equivalents will be sufficient to fund our business operations for the foreseeable future. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Our loan under the Paycheck Protection Program may not be forgiven or may subject us to challenges and investigations regarding qualification for the loan.

We have received loan proceeds in the amount of approximately $1.8 million under the PPP, which was established under the CARES Act and is administered by the SBA. Under the terms of the CARES Act, PPP loan recipients can apply for loan forgiveness. The potential loan forgiveness for all or a portion of PPP loans is determined, subject to limitations, based on the use of loan proceeds over the 24 weeks after the loan proceeds are disbursed for payment of payroll costs and any payments of mortgage interest, rent, and utilities. The amount of loan forgiveness will be reduced if PPP loan recipients terminate employees or reduce salaries during the covered period. The unforgiven portion of our PPP Loan, if any, is payable over two years at an interest rate of 1%, with a deferral of principal and interest payments to either (i) the date that the SBA remits the borrower's loan forgiveness amount to the lender or (ii) if the borrower does not apply for forgiveness, 10 months after the end of the borrower's loan forgiveness covered period. We believe that we have used the proceeds from the PPP Loan for purposes consistent with the PPP. While we currently believe that our use of the loan proceeds will meet the conditions for forgiveness of the PPP Loan, there can be no assurance that forgiveness for any portion of the PPP Loan will be obtained.

Additionally, the PPP loan application required us to certify that the current economic uncertainty made the PPP loan request necessary to support our ongoing operations. While we made this certification in good faith after analyzing, among other things, our financial situation and access to alternative forms of capital, and believe that we satisfied all eligibility criteria for the PPP loans and that our receipt of the PPP loans is consistent with the broad objectives of the Paycheck Protection Program of the CARES Act, the certification described above contains subjective criteria and is subject to interpretation. In addition, the SBA has stated that it is unlikely that a public company with substantial market value and access to capital markets will be able to make the required certification in good faith. The lack of clarity regarding loan eligibility under the program has resulted in significant media coverage and controversy with respect to public companies applying for and receiving loans. If, despite our good faith belief that we satisfied all eligibility requirements for the PPP loan, the SBA concludes we have been ineligible to receive the PPP loan or in violation of any of the laws or regulations that apply to us in connection with the PPP loan, including the False Claims Act, we may be subject to penalties, including significant civil, criminal, and administrative penalties and could be required to repay the PPP loan. In the event that we seek forgiveness of all or a portion of the PPP Loan, we will also be required to make certain certifications that will be subject to audit and review by government entities and could subject us to significant penalties and liabilities if found to be inaccurate. In addition, a review or audit by the SBA or other government entity or claims under the False Claims Act could consume significant financial and management resources. Any of these events could harm our business, results of operations or financial condition.

We do not have significant operating revenue and may never achieve profitability.

To date, we have funded our operations primarily through public offerings of our common stock. Our ability to achieve significant revenue or profitability depends upon our ability to complete the development of our drug candidates, to develop and obtain patent protection and regulatory approvals for our drug candidates and to manufacture and commercialize the resulting drugs. We are not expecting any significant revenues in the short-term from our products or product candidates. Furthermore, we may not be able to ever successfully identify, develop, commercialize, patent, manufacture, obtain required regulatory approvals or market any products. Moreover, even if we do identify, develop, commercialize, patent, manufacture, or obtain required regulatory approvals to market additional products, we may not generate revenues or royalties from commercial sales of these products for a significant number of years, if at all. Therefore, our operations are subject to all the risks inherent in the establishment of a new business enterprise. In the next few years, we expect limited revenues from product sales, if any, and any amounts that we receive under strategic partnerships and research or drug development collaborations that we may establish and, as a result, we may be unable to achieve or maintain profitability in the future or to achieve significant revenues in order to fund our operations.

Failure to achieve and maintain effective internal controls could have a material adverse effect on our business.

Effective internal controls are necessary for us to provide reliable financial reports. If we cannot provide reliable financial reports, our operating results could be harmed. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our operating results, or cause us to fail to meet our reporting obligations. Failure to achieve and maintain an effective internal control environment could cause investors to lose confidence in our reported financial information, which could have a material adverse effect on our stock price. Failure to comply with Section 404 of the Sarbanes-Oxley Act could also potentially subject us to actions or investigations by the SEC or other regulatory authorities.

We expect to continue to need to raise additional capital to operate our business, and our failure to obtain funding when needed or on terms that are favorable to us may force us to delay, reduce or eliminate our development programs or aspects thereof.

We will need to raise additional capital to fund our future operations and we cannot be certain that funding will be available to us on acceptable terms on a timely basis, or at all. Our ability to raise capital through the sale of securities may be limited by our number of authorized shares of common stock and various rules of the SEC and the Nasdaq that place limits on the number and dollar amount of securities that we may sell. If we fail to raise additional funds on acceptable terms or at all, we may be unable to complete planned preclinical and clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to delay, discontinue, or curtail product development, or forego licensing in attractive business opportunities. Any additional sources of financing will likely involve the issuance of our equity or debt securities, which will have a dilutive effect on our stockholders.

Risks related to our common stock

The market price of our common stock may be volatile and adversely affected by several factors.

The market price of our common stock could fluctuate significantly in response to various factors and events, including:

- our ability to integrate operations, technology, products, and services;
- our ability to execute our business plan;
- operating results below expectations;
- announcements concerning product development results, including clinical trial results;
- regulatory or legal developments in the U.S. or EU, including decisions from regulatory agencies relating to our product candidates;
- litigation or public concern about the safety of our potential products;
- our issuance of additional securities, including debt or equity or a combination thereof, which will be necessary to fund our operating expenses;
- announcements of technological innovations or new products by us or our competitors;
- loss of any strategic relationship;
- industry developments, including, without limitation, changes in healthcare policies or practices or third-party reimbursement policies;
- economic and other external factors;
- period-to-period fluctuations in our financial results; and
- whether an active trading market in our common stock develops and is maintained.

In addition, the securities markets have from time-to-time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of our common stock.

Raising additional funds by issuing securities or through licensing or lending arrangements or through our at-the-market sale agreement may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish proprietary rights.

If we raise additional capital by issuing equity securities, the share ownership of existing stockholders will be diluted. Any future debt financing may involve covenants that, among other restrictions, limit our ability to incur liens or additional debt, pay dividends, redeem, or repurchase our common stock, make certain investments or engage in certain merger, consolidation, or asset sale transactions. In addition, if we raise additional funds through licensing arrangements or the disposition of any of our assets, it may be necessary to relinquish potentially valuable rights to our product candidates or grant licenses on terms that are not favorable to us.

The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. We may sell shares or other securities in other offerings, including under our open market sale agreement with Jefferies, at a price per share that is less than the prices per share paid by other investors, and investors purchasing shares of our common stock or other securities in the future could have rights superior to existing stockholders. The sale of additional equity or convertible securities would dilute all of our stockholders and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders. For example, we raised capital through a public offering of equity securities and pre-funded warrants in December 2019 pursuant to which existing stockholders incurred immediate dilution of $1.10 per share in as-adjusted net tangible book value of common stock as a result of such offering.

We have not paid cash dividends in the past and do not expect to pay cash dividends in the foreseeable future. Any return on investment may be limited to the value of our common stock.

We have never paid cash dividends on our common stock and do not anticipate paying cash dividends on our common stock in the foreseeable future. The payment of dividends on our capital stock will depend on our earnings, financial condition and other business and economic factors affecting us at such time as the board of directors may consider relevant. If we do not pay dividends, our common stock may be less valuable because a return on stockholder investment will only occur if the common stock price appreciates.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit or arbitration in which we are, or may become, involved;
- regulatory developments affecting our product candidates; and
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our common stock to fluctuate substantially.

Provisions of our charter documents could discourage an acquisition of our company that would benefit our stockholders and may have the effect of entrenching, and making it difficult to remove, management.

Provisions of our Certificate of Incorporation and Bylaws may make it more difficult for a third party to acquire control of us, even if a change in control would benefit our stockholders. In particular, shares of our preferred stock may be issued in the future without further stockholder approval and upon such terms and conditions, and having such rights, privileges and preferences, as our Board of Directors may determine, including, for example, rights to convert into our common stock. The rights of the holders of our common stock will be subject to, and may be adversely affected by, the rights of the holders of any of our preferred stock that may be issued in the future. The issuance of our preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire control of us. This could limit the price that certain investors might be willing to pay in the future for shares of our common stock and discourage these investors from acquiring a majority of our common stock. Further, the existence of these corporate governance provisions could have the effect of entrenching management and making it more difficult to change our management.

There can be no assurance that we will be able to comply with continued listing standards of the Nasdaq Capital Market.

The Nasdaq Capital Market's continued listing standards for our common stock require, among other things, that (i) we maintain a closing bid price for our common stock of at least $1.00, and (ii) we maintain: (A) stockholders' equity of $2.5 million; (B) market value of listed securities of $35 million; or (C) net income from continuing operations of $500,000 in the most recently completed fiscal year or in two of the last three most recently completed fiscal years. Any failures to satisfy any continued listing requirements could lead to the receipt of a deficiency notice from the Nasdaq and ultimately to a delisting from trading of our common stock. We cannot be certain that we will be able to continue to comply with the minimum bid price and the other standards that we are required to meet in order to maintain a listing of our common stock on the Nasdaq Capital Market. Our failure to continue to meet these requirements may result in our common stock being delisted from the Nasdaq Capital Market. If our common stock were delisted from the Nasdaq Capital Market, among other things, this could result in a number of negative implications, including reduced liquidity in our common stock as a result of the loss of market efficiencies associated with the Nasdaq and the loss of federal preemption of state securities laws as well as the potential loss of confidence by suppliers, customers and employees, institutional investor interest, fewer business development opportunities, greater difficulty in obtaining financing and breaches of certain contractual obligations.

As a result of the resignations of Stefano Buono, Stephen B. Howell, M.D., George Migausky, and Shawn Tomasello as members of the Board of Directors as of September 27, 2020, the Company does not at present comply with the Nasdaq Capital Market rules requiring (i) a Board of Directors comprised of a majority of independent directors and (ii) a three-member audit committee comprised only of independent directors. The Company has until the earlier of the Company's next annual shareholder meeting or September 27, 2021 to regain compliance.

Our ability to use our net operating loss carry forwards may be subject to limitation.

Generally, a change of more than 50% in the ownership of a company's stock, by value, over a three-year period constitutes an ownership change for U.S. federal income tax purposes. An ownership change may limit our ability to use our net operating loss carryforwards attributable to the period prior to the change. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability for us. As of December 31, 2020, we had net operating loss carryforwards aggregating approximately $290.8 million.

Ownership of our shares is concentrated in the hands of a few investors, which could limit the ability of our other stockholders to influence the direction of the Company.

As calculated by the SEC rules of beneficial ownership, SCO Capital Partners LLC and affiliates ("SCO Capital") beneficially owned approximately 14% of our common stock as of March 19, 2021. SCO Capital also has the right to nominate two individuals to serve as members of the Board pursuant to a director designation agreement dated as of November 15, 2007 between Abeona and SCO. Accordingly, SCO Capital has the ability to significantly influence or determine the election of our directors or the outcome of most corporate actions requiring stockholder approval. They may exercise this ability in a manner that advances their best interests and not necessarily those of our other stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not Applicable.

ITEM 2. PROPERTIES

Our corporate headquarters is located in New York, New York, where we currently lease 10,400 square feet of office space. That lease expires in January 2026. We also lease 45,300 square feet of manufacturing, laboratory and office space in Cleveland, Ohio. That lease expires in December 2025. We lease 1,700 square feet of office space in Madrid, Spain. That lease expires in September 2021; we expect to renew this lease before it expires. We believe that our facilities are sufficient to meet our current needs and that suitable space will be available as and when needed.

ITEM 3. LEGAL PROCEEDINGS

We are currently engaged in an arbitration proceeding with REGENXBIO regarding the former license agreement between the parties relating to use of the AAV9 capsid in our MPS IIIA, MPS IIIB, CLN1, and CLN3 programs. The license terminated on May 2, 2020, and on May 25, 2020, we filed an arbitration claim with the American Arbitration Association ("AAA") alleging that REGENXBIO materially breached the license agreement prior to termination and seeking, among other things, a declaration that as a result of REGENXBIO's material breach, we are not responsible for payments totaling $28 million (which would otherwise have been due in 2020) plus accrued interest ($3.5 million as of December 31, 2020). REGENXBIO disputes our arbitration claim and has filed a counterclaim seeking payment of these amounts. An arbitration hearing before a tribunal of three AAA arbitrators was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM **5.** MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock has traded on the Nasdaq Capital Market ("Nasdaq") under the symbol "ABEO" since June 22, 2015.

We have never declared or paid any cash dividends on our common stock and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. The payment of dividends, if any, in the future is within the discretion of our Board of Directors and will depend on our earnings, capital requirements and financial condition and other relevant facts. We currently intend to retain all future earnings, if any, to finance the development and growth of our business.

The number of record holders of our common stock as of March 19, 2021 was approximately 170.

Equity Compensation Plan Information

The following table sets forth, as of December 31, 2020, information about shares of common stock outstanding and available for issuance under our existing equity compensation plans.

Plan Category	**Number of securities to be issued upon exercise of outstanding options, warrants and rights**	**Weighted-average exercise price of outstanding options, warrants and rights**	**Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))**
	(a)	**(b)**	**(c)**
Equity compensation plans approved by security holders:			
2015 Equity Incentive Plan	5,560,739	$ 2.21	6,339,370
2005 Equity Incentive Plan	124,800	8.55	-
Equity compensation plans not approved by security holders	-	-	-
Total	5,685,539	$ 2.35	6,339,370

Issuer Repurchases of Equity Securities

None.

Recent Sales of Unregistered Securities

None.

ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion should be read in conjunction with our consolidated financial statements and related notes included in this Form 10-K.

Abeona is a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases. Our lead clinical programs consist of: (i) EB-101, an autologous, gene-corrected cell therapy for recessive dystrophic epidermolysis bullosa ("RDEB"), (ii) ABO-102, an adeno-associated virus ("AAV")-based gene therapy for Sanfilippo syndrome type A ("MPS IIIA"), and (iii) ABO-101, an AAV-based gene therapy for Sanfilippo syndrome type B ("MPS IIIB"). We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases and next-generation AAV-based gene therapies using the novel AIM™ capsid platform that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs.

IMPACT OF COVID-19 PANDEMIC ON OUR BUSINESS

We continue to assess the evolving impact of the COVID-19 pandemic on our business and take appropriate actions to manage our spending activities and preserve our cash resources. We continue to actively monitor the situation and may take further actions to adjust our business operations that we determine are in the best interests of our patients, employees, suppliers and stockholders. While we are unable to determine or predict the extent, duration or scope of the overall impact the COVID-19 pandemic will have on our business, operations, financial condition or liquidity, we believe it is important to keep our stakeholders informed about how our response to COVID-19 is progressing and how our operations and financial condition may change.

Clinical Program Activities

We remain committed to advancing our clinical programs and have implemented measures to minimize disruption. We also are regularly reassessing plans along with associated processes and policies to ensure our patients and employees are safe, and that continuity in our operations remains.

All current clinical trial sites are active. We are also providing virtual and remote follow-up to ensure compliance with safety oversight. In June 2020, we resumed patient enrollment in our Phase 3 VIITAL™ study of EB-101 after the study was paused in March 2020 to ensure the safety of study participants and site staff during the pandemic. The ongoing Phase 1/2 clinical trials of our investigational AAV-based gene therapies for MPS IIIA and IIIB (ABO-102 and ABO-101, respectively) have continued to treat patients.

Manufacturing Activities

Operations at our Cleveland manufacturing facility were significantly scaled back from March 2020 until early June 2020 to ensure the safety of employees and those around them, and to accommodate reduced manufacturing and clinical development activities. We had paused our manufacturing activities for EB-101 clinical material, pending patient enrollment, as well as our AAV manufacturing and process development activities. During this pause period, we took the opportunity to complete maintenance and monitoring projects.

In June 2020, we resumed our EB-101 manufacturing activities, including process development for the internal production of retrovirus as well as our AAV process development and manufacturing activities.

Business Operations

Many of the additional protective measures we instituted during the first quarter of 2020 in response to the COVID-19 pandemic remain in place, and we continue to regularly assess and improve our safety practices and policies.

The extent of the impact of the COVID-19 pandemic on our business, operations, and clinical trials continues to evolve and will depend on certain developments, including: (i) the duration of the declared health emergencies; (ii) future actions taken by governmental authorities and regulators with respect to the pandemic, including reinstituting state and local lockdowns; (iii) the impact on our partners, collaborators, and suppliers; and (iv) actions being taken by us in response to this crisis. We remain dedicated to communicating regularly and openly with our stakeholders as more information becomes available, including updates on material changes to prior guidance as we continue to follow applicable government, regulatory and institutional guidelines.

RESULTS OF OPERATIONS

Comparison of Years Ended December 31, 2020 and December 31, 2019

License and other revenues for the year ended December 31, 2020 were $10.0 million, as compared to nil for the same period of 2019. The increase in revenue was due to sublicense and inventory purchase agreements we entered into with Taysha Gene Therapies ("Taysha") in August 2020 for ABO-202, an AAV gene therapy for CLN1 disease (also known as infantile Batten disease) and a sublicense agreement we entered into with Taysha in October 2020 for a gene therapy for Rett syndrome and MECP2 gene constructs and regulation of their expression. The agreements grant to Taysha worldwide exclusive rights to intellectual property developed by scientists at the University of North Carolina at Chapel Hill, the University of Edinburgh and us, and our know-how relating to the research, development and manufacture of the gene therapies for CLN1 and Rett syndrome.

Total research and development spending for the year ended December 31, 2020 was $30.1 million, as compared to $48.6 million for the same period of 2019, a decrease of $18.5 million. The decrease in expenses was primarily due to:

- decreased clinical and development work for our gene and cell therapy product candidates ($16.3 million), due to scaled back manufacturing, clinical and non-clinical development activities resulting from the effects of the COVID-19 pandemic, as well as cost savings from the decision to internally manufacture retrovirus for the EB-101 program;
- decreased salary and related costs ($1.7 million);
- decreased employee travel and related expenses ($0.3 million); and
- decreases in net other research and development spending ($0.2 million).

Total general and administrative expenses were $23.8 million for the year ended December 31, 2020, as compared to $20.7 million for the same period of 2019, an increase of $3.1 million. The increase in expenses was due primarily to the following:

- increased salary and related costs ($1.8 million), including severance costs associated with management changes;
- increased professional fees ($1.0 million); and
- increases in net other general and administrative expenses ($0.3 million).

Depreciation and amortization was $4.6 million for the year ended December 31, 2020, as compared to $7.8 million for the same period in 2019, a decrease of $3.2 million. The decrease was driven primarily by decreased amortization expense on licensed technology due to the write-off of the REGENXBIO licensed technology in the first quarter of 2020.

Our license agreement with REGENXBIO terminated on May 2, 2020. Since our impairment testing indicated that the carrying value of the license agreement with REGENXBIO exceeded its fair value, we recorded a $32.9 million non-cash impairment charge during the year ended December 31, 2020.

Interest and miscellaneous income was $1.3 million for the year ended December 31, 2020, as compared to $1.2 million of the same period in 2019.

Interest and other expense was $4.1 million for the year ended December 31, 2020, as compared to $0.4 million for the same period of 2019. The increase results primarily from accrued interest on the amounts that we may owe to REGENXBIO under the prior license agreement, which amount is subject to the arbitration discussed in Note 4 of Notes to Consolidated Financial Statements in Part II, Item 8. As described in more detail in Note 4, we have filed an arbitration claim alleging that REGENXBIO materially breached the license agreement and seeking, among other things, a declaration that we are not responsible for such payments.

Net loss for the year ended December 31, 2020 was $84.2 million, or a $0.91 basic and diluted loss per common share as compared to a net loss of $76.3 million, or a $1.51 basic and diluted loss per common share, for the same period in 2019. The increase in the net loss results primarily from the licensed technology impairment charge of $32.9 million, partially offset by increased license and other revenues along with decreased clinical and development expenses.

Liquidity and Capital Resources

We have historically funded our operations primarily through sales of common stock. The COVID-19 pandemic has negatively affected the global economy and created significant volatility and disruption of financial markets. An extended period of economic disruption could negatively affect our business, financial condition, and access to sources of liquidity.

Our principal source of liquidity is cash, cash equivalents and short-term investments. As of December 31, 2020 and 2019, our cash, cash equivalents and short-term investments were $95.0 million and $129.3 million, respectively. Based upon our current operating plans, we believe that we have sufficient resources to fund operations through at least the next 12 months with our existing cash, cash equivalents and short-term investments. We will need to secure additional funding in the future, to carry out all our planned research and development activities. If we are unable to obtain additional financing or generate license or product revenue, the lack of liquidity and sufficient capital resources could have a material adverse effect on our future prospects.

As of December 31, 2020 and 2019, our working capital was $55.8 million and $93.7 million, respectively. The decrease in working capital resulted primarily from $35.0 million of cash used for operating activities during the year ended December 31, 2020.

On May 2, 2020, we received loan proceeds in the amount of approximately $1.8 million (the “PPP Loan”) under the Paycheck Protection Program (“PPP”). The PPP was established under the Coronavirus Aid, Relief and Economic Security Act, as amended (“CARES Act”), and is administered by the U.S. Small Business Administration (“SBA”). Under the terms of the CARES Act, PPP loan recipients can apply for loan forgiveness. The potential loan forgiveness for all or a portion of PPP loans is determined, subject to limitations, based on the use of loan proceeds over the 24 weeks after the loan proceeds are disbursed. The amount of loan forgiveness will be reduced if PPP loan recipients terminate employees or reduce salaries during the covered period. The unforgiven portion of our PPP Loan, if any, is payable over two years at an interest rate of 1%, with a deferral of principal and interest payments to either (i) the date that the SBA remits the borrower’s loan forgiveness amount to the lender or (ii) if the borrower does not apply for forgiveness, 10 months after the end of the borrower’s loan forgiveness covered period. We believe that we have used the proceeds from our PPP Loan for purposes consistent with the PPP. While we currently believe that our use of the loan proceeds will meet the conditions for forgiveness of our PPP Loan, there can be no assurance that forgiveness for any portion of the PPP Loan will be obtained.

On December 24, 2019, we closed an underwritten public offering of 32,382,945 shares of common stock at a public offering price of $2.50 per share. In addition, as part of the offering, we sold "pre-funded" warrants to purchase up to an aggregate of 9,017,055 shares of common stock at a purchase price of $2.4999 per pre-funded warrant, which equals the public offering price per share of the common stock less the $0.0001 per share exercise price of each pre-funded warrant. The gross proceeds to the Company were approximately $103.5 million, before deducting the underwriting discounts and commissions and estimated offering expenses payable by the Company. In October 2020, all of the pre-funded warrants were exercised and converted into shares of common stock.

On August 17, 2018, we entered into an open market sale agreement with Jefferies LLC. Pursuant to the terms of this agreement, we may sell from time to time, through Jefferies LLC, shares of our common stock for an aggregate sales price of up to $150 million. Any sales of shares pursuant to this agreement are made under our effective "shelf" registration statement on Form S-3 that is on file with and has been declared effective by the SEC. We did not sell any shares of our common stock under this agreement during the year ended December 31, 2020. During the year ended December 31, 2019, we sold 3,086,950 shares of our common stock under this agreement and received $17.0 million of proceeds.

License Agreement

On November 4, 2018, we entered into a license agreement with REGENXBIO to obtain rights to an exclusive worldwide license (subject to certain non-exclusive rights previously granted for MPS IIIA), with rights to sublicense, to REGENXBIO's NAV AAV9 vector for gene therapies for treating MPS IIIA, MPS IIIB, CLN1 Disease and CLN3 Disease. Consideration for the rights granted under the original agreement included fees totaling $180 million and a running royalty on net sales, including: (i) an initial fee of $20 million, $10 million of which was due to REGENXBIO shortly after the effective date of the agreement, and $10 million of which was to be due on the first anniversary of the effective date of the agreement in November 2019, (ii) annual fees totaling up to $100 million, payable in $20 million annual installments beginning on the second anniversary of the effective date (the first of which was to remain payable if the agreement were terminated before the second anniversary in November 2020), (iii) sales milestone payments totaling $60 million, and (iv) royalties payable in the low double digits to low teens on net sales of products covered under the agreement. The license was being amortized over the life of the patent of eight years. On November 1, 2019, we entered into an amendment of the original license agreement. The amended agreement replaced the $10 million payment due on November 4, 2019 with a $3 million payment due on November 4, 2019 and an additional $8 million payment (which included $1 million of interest) that would have been due no later than April 1, 2020. That $8 million payment had been scheduled to be paid by April 1, 2020 and the $20 million that had been due to be paid on November 4, 2020, and both were recorded as payable to licensor on the consolidated balance sheet. The Company has disputed that it is responsible for the $8 million and $20 million payments, and those payments are the subject of a current arbitration between the Company and REGENXBIO.

Prior to the April 1, 2020 deadline, we engaged REGENXBIO in discussions in an attempt to renegotiate the financial terms of the agreement, but we were unable to reach a mutual understanding that we believed would have been favorable for the Company or our programs, and we did not make the $8 million payment due by April 1, 2020. On April 17, 2020, REGENXBIO sent us a written demand for the $8 million fee, payable within a 15-day cure period after receipt of the demand letter. The license terminated on May 2, 2020, when the 15-day period expired. There were no penalties for early termination of the license. On May 25, 2020, we filed an arbitration claim with the American Arbitration Association ("AAA") alleging that REGENXBIO materially breached the license agreement prior to termination and seeking, among other things, a declaration that as a result of REGENXBIO's material breach, we are not responsible for payments totaling $28 million (which would otherwise have been due in 2020) plus accrued interest (of $3.5 million as of December 31, 2020). REGENXBIO disputes our arbitration claim and has filed a counterclaim seeking payment of the $28 million plus interest, which REGENXBIO argues remains due. An arbitration hearing before a tribunal of three AAA arbitrators was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021. For additional information, refer to Part I, Item 3. Legal Proceedings of this Form 10-K.

Since our inception, we have incurred negative cash flows from operations and have expended, and expect to continue to expend, substantial funds to complete our planned product development efforts. We have not been profitable since inception and to date have received limited revenues from the sale of products. We expect to incur losses for the next several years as we continue to invest in product research and development, preclinical studies, clinical trials, and regulatory compliance and cannot provide assurance that we will ever be able to generate sufficient product sales or royalty revenue to achieve profitability on a sustained basis, or at all.

If we raise additional funds by selling additional equity securities, the relative equity ownership of our existing investors will be diluted, and the new investors could obtain terms more favorable than previous investors. If we raise additional funds through 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 or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates to third parties that we would otherwise prefer to develop and market ourselves.

We are carefully and continually reassessing key business activities and all associated spending decisions as the COVID-19 pandemic continues to evolve. Nonetheless, we are spending necessary funds on manufacturing activities and preclinical studies and clinical trials of potential products, including research and development with respect to our acquired and developed technology. Our future capital requirements and adequacy of available funds depend on many factors, including:

- the evolving impact to our business, operations, and clinical programs from the COVID-19 pandemic and related effects on the U.S. and global economy;
- the successful development and commercialization of our gene and cell therapy and other product candidates;
- the ability to establish and maintain collaborative arrangements with corporate partners for the research, development, and commercialization of products;
- continued scientific progress in our research and development programs;
- the magnitude, scope and results of preclinical testing and clinical trials;
- the costs involved in filing, prosecuting, and enforcing patent claims;
- the costs involved in conducting clinical trials;
- competing technological developments;
- the cost of manufacturing and scale-up;
- the ability to establish and maintain effective commercialization arrangements and activities; and
- the successful outcome of our regulatory filings.

Due to uncertainties and certain of the risks described above, including those relating to the COVID-19 pandemic, our ability to successfully commercialize our product candidates, our ability to obtain applicable regulatory approval to market our product candidates, our ability to obtain necessary additional capital to fund operations in the future, our ability to successfully manufacture our products and our product candidates in clinical quantities or for commercial purposes, government regulation to which we are subject, the uncertainty associated with preclinical and clinical testing, intense competition that we face, market acceptance of our products, the potential necessity of licensing technology from third parties and protection of our intellectual property, it is not possible to reliably predict future spending or time to completion by project or product category or the period in which material net cash inflows from significant projects are expected to commence. If we are unable to timely complete a particular project, our research and development efforts could be delayed or reduced, our business could suffer depending on the significance of the project and we might need to raise additional capital to fund operations, as discussed in the risks above.

We plan to continue our policy of investing any available funds in suitable certificates of deposit, money market funds, government securities and investment-grade, interest-bearing securities. We do not invest in derivative financial instruments.

Contractual Obligations

The following table summarizes our significant contractual obligations as of the payment due date by period as of December 31, 2020:

	Payments Due by Period				
	Less than 1 year	1 to 3 years	4 to 5 years	After 5 years	Total
Operating leases	$ 1,713,000	$ 3,468,000	$ 3,580,000	$ 87,000	$ 8,848,000
Payable to licensor	31,515,000	-	-	-	31,515,000

We enter into agreements in the normal course of business with clinical research organizations for clinical trials and clinical manufacturing organizations for supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. These contractual obligations are cancelable at any time by us, generally upon prior written notice to the vendor, and are thus not included in the contractual obligations table.

Operating lease amounts represent future minimum lease payments under our non-cancelable operating lease agreements. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

On November 4, 2018, we entered into a license agreement with REGENXBIO to obtain rights to an exclusive worldwide license (subject to certain non-exclusive rights previously granted for MPS IIIA), with rights to sublicense, to REGENXBIO's NAV AAV9 vector for gene therapies for treating MPS IIIA, MPS IIIB, CLN1 Disease and CLN3 Disease. Consideration for the rights granted under the original agreement included fees totaling $180 million and a running royalty on net sales, including: (i) an initial fee of $20 million, $10 million of which was due to REGENXBIO shortly after the effective date of the agreement, and $10 million of which was to be due on the first anniversary of the effective date of the agreement in November 2019, (ii) annual fees totaling up to $100 million, payable in $20 million annual installments beginning on the second anniversary of the effective date (the first of which was to remain payable if the agreement were terminated before the second anniversary in November 2020), (iii) sales milestone payments totaling $60 million, and (iv) royalties payable in the low double digits to low teens on net sales of products covered under the agreement. On November 1, 2019, we entered into an amendment of the original license agreement. The amended agreement replaced the $10 million payment due on November 4, 2019 with a $3 million payment due on November 4, 2019 and an additional $8 million payment (which included $1 million of interest) that would have been due no later than April 1, 2020. That $8 million payment had been scheduled to be paid by April 1, 2020 and the $20 million that had been due to be paid on November 4, 2020, and both were recorded as payable to licensor on the consolidated balance sheet. The Company has disputed that it is responsible for the $8 million and $20 million payments, and those payments are the subject of a current arbitration between the Company and REGENXBIO.

Prior to the April 1, 2020 deadline, we engaged REGENXBIO in discussions in an attempt to renegotiate the financial terms of the agreement, but we were unable to reach a mutual understanding that we believed would have been favorable for the Company or our programs, and we did not make the $8 million payment due by April 1, 2020. On April 17, 2020, REGENXBIO sent us a written demand for the $8 million fee, payable within a 15-day cure period after receipt of the demand letter. The license terminated on May 2, 2020, when the 15-day period expired. There were no penalties for early termination of the license. On May 25, 2020, we filed an arbitration claim with the American Arbitration Association ("AAA") alleging that REGENXBIO materially breached the license agreement prior to termination and seeking, among other things, a declaration that as a result of REGENXBIO's material breach, we are not responsible for payments totaling $28 million (which would otherwise have been due in 2020) plus accrued interest (of $3.5 million as of December 31, 2020). REGENXBIO disputes our arbitration claim and has filed a counterclaim seeking payment of the $28 million plus interest, which REGENXBIO argues remains due. An arbitration hearing before a tribunal of three AAA arbitrators was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021. For additional information, refer to Part I, Item 3. Legal Proceedings of this Form 10-K.

In addition, we are also party to other license agreements, which include contingent payments. However, contingent payments related to these license agreements are not disclosed as the satisfaction of these contingent payments is uncertain as of December 31, 2020 and, if satisfied, the timing of payment for these amounts was not reasonably estimable as of December 31, 2020. Commitments related to the license agreements include contingent payments that will become payable if and when certain development, regulatory and commercial milestones are achieved. During the next 12 months, we do not expect to make milestone payments related to such license agreements.

Critical Accounting Estimates

The preparation of our consolidated financial statements in conformity with accounting principles generally accepted in the U.S. requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenues and expenses during the reported period. In applying our accounting principles, we must often make individual estimates and assumptions regarding expected outcomes or uncertainties. As one might expect, the actual results or outcomes are often different than the estimated or assumed amounts. These differences are usually minor and are included in our consolidated financial statements as soon as they are known. Our estimates, judgments and assumptions are continually evaluated based on available information and experience. Because of the use of estimates inherent in the financial reporting process, actual results could differ from those estimates.

Leases

Effective January 1, 2019, we adopted the provisions of ASU 2016-02, *Leases*, as amended ("ASC 842") using the cumulative-effect adjustment transition method, which applies the provisions of the standard as of the effective date without adjusting the comparative periods presented. ASC 842 requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under the previous guidance of ASC 840, *Leases*. As a result of the adoption, we recorded operating lease right-of-use assets of $8.9 million and operating lease liabilities of $8.9 million. The adoption had an immaterial impact on our net assets as of January 1, 2019. In addition, we elected the package of practical expedients permitted under the transition guidance within the new standard, which allowed us to carry forward the historical lease classification.

We determine if an arrangement is a lease at inception. Right-of-use lease assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. The classification of our leases as operating or finance leases along with the initial measurement and recognition of the associated right-of-use assets and lease liabilities is performed at the lease commencement date. The measurement of lease liabilities is based on the present value of future lease payments over the lease term. As our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. The right-of-use asset is based on the measurement of the lease liability and includes any lease payments made prior to or on lease commencement and excludes lease incentives and initial direct costs incurred, as applicable. Rent expense for our operating leases is recognized on a straight-line basis over the lease term. We do not have any leases classified as finance leases.

Our leases do not have significant rent escalation, holidays, concessions, material residual value guarantees, material restrictive covenants or contingent rent provisions. Our leases include both lease (e.g., fixed payments including rent, taxes, and insurance costs) and non-lease components (e.g., common-area or other maintenance costs), which are accounted for as a single lease component as we have elected the practical expedient to group lease and non-lease components for all leases. We have also elected the practical expedient to exclude short-term leases from our right-of-use assets and lease liabilities.

Most leases include one or more options to renew. The exercise of lease renewal options is typically at our sole discretion; therefore, the majority of renewals to extend the lease terms are not included in our right-of-use assets and lease liabilities as they are not reasonably certain of exercise. We regularly evaluate the renewal options and when they are reasonably certain of exercise, we include the renewal period in our lease term.

Licensed Technology

We maintain licensed technology on our consolidated balance sheet until either the licensed technology agreement underlying it is completed or the asset becomes impaired. When we determine that an asset has become impaired or we abandon a project, we write down the carrying value of the related intangible asset to its fair value and take an impairment charge in the period in which the impairment occurs.

Generally, licensed technology is amortized over the life of the patent or the agreement. We test our intangible assets for impairment on an annual basis, or more frequently if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding our drug candidate or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate or new information regarding potential sales for the drug. In connection with each annual impairment assessment and any interim impairment assessment, we compare the fair value of the asset as of the date of the assessment with the carrying value of the asset on our consolidated balance sheet.

We considered the status of our discussions with REGENXBIO in March 2020 as a potential indicator of impairment in accordance with ASC 360-10-35-21. Our impairment test indicated that the carrying value of the license agreement exceeded its fair value and we recorded a $32.9 million non-cash impairment charge in 2020.

In 2019, we did not impair any licensed technology.

Goodwill

As of December 31, 2020 and 2019, we recorded goodwill of $32.5 million on our consolidated balance sheet. In accordance with ASC 350 — *Intangibles — Goodwill and Other,* goodwill is tested annually for impairment and whenever changes in circumstances occur that would indicate impairment.

In 2020 and 2019, we did not impair any goodwill.

Revenue Recognition

Effective January 1, 2018, we adopted ASU 2014-09, *Revenue from Contracts with Customers*, as amended ("ASC 606"), using the modified retrospective transition method. The ASC 606 revenue recognition standard replaced the prior revenue recognition standard ASC 605, *Revenue Recognition*. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with our customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation.

Sublicense and Inventory Purchase Agreements Relating to CLN1 Disease: In August 2020, we entered into sublicense and inventory purchase agreements with Taysha Gene Therapies ("Taysha") relating to a potential gene therapy for CLN1 disease. Under the sublicense agreement, Taysha received worldwide exclusive rights to intellectual property and know-how relating to the research, development, and manufacture of the potential gene therapy, which we had referred to as ABO-202. Under the inventory purchase agreement, we sold to Taysha certain inventory and other items related to ABO-202. We assessed these contracts at contract inception and determined that, under ASC 606, the two contracts would be combined and accounted for as a single contract, with a single performance obligation. We assessed the nature of the promised license to determine whether the license has significant stand-alone functionality and evaluated whether such functionality can be retained without ongoing activities by us and determined that the license has significant stand-alone functionality. Furthermore, we have no ongoing activities associated with the license to support or maintain the license's utility. Based on this, we determined that the pattern of transfer of control of the license to Taysha was at a point in time.

The transaction price of the contract includes (i) $7.0 million of fixed consideration, (ii) up to $26.0 million of variable consideration in the form of event-based milestone payments, (iii) up to $30.0 million of variable consideration in the form of sales-based milestone payments, and (iv) other royalty-based payments based on net sales. The event-based milestone payments are based on certain development and regulatory events occurring. We evaluated whether the milestone conditions have been achieved and if it is probable that a significant revenue reversal would not occur before recognizing the associated revenue. We determined that these milestone payments are not within our control or the licensee's control, such as regulatory approvals, and are not considered probable of being achieved until those approvals are received. Accordingly, we have fully constrained the $26.0 million of event-based milestone payments until such time that it is probable that significant revenue reversal would not occur. The sales-based milestone payments and other royalty-based payments are based on a level of sales for which the license is deemed to be the predominant item to which the royalties relate. We will recognize revenue for these payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, we have not recognized any sales-based or royalty revenue resulting from this licensing arrangement.

Under this arrangement, we recognized $7.0 million of revenue during the year ended December 31, 2020, which amount related solely to fixed consideration. We do not have any contract assets or contract liabilities as a result of this transaction.

Sublicense Agreement Relating to Rett Syndrome: In October 2020, we entered into a sublicense agreement with Taysha for a gene therapy for Rett syndrome and MECP2 gene constructs and regulation of their expression. The agreement grants Taysha worldwide exclusive rights to intellectual property developed by scientists at the University of North Carolina at Chapel Hill, the University of Edinburgh and us, and our know-how relating to the research, development, and manufacture of the gene therapy for Rett syndrome and MECP2 gene constructs and regulation of their expression.

We assessed the nature of the promised license to determine whether the license has significant stand-alone functionality and evaluated whether such functionality can be retained without ongoing activities by us and determined that the license has significant stand-alone functionality. Furthermore, we have no ongoing activities associated with the license to support or maintain the license's utility. Based on this, we determined that the pattern of transfer of control of the license to Taysha was at a point in time.

The transaction price of the contract includes (i) $3.0 million of fixed consideration, (ii) up to $26.5 million of variable consideration in the form of event-based milestone payments, (iii) up to $30.0 million of variable consideration in the form of sales-based milestone payments, and (iv) other royalty-based payments based on net sales. The event-based milestone payments are based on certain development and regulatory events occurring. We evaluated whether the milestone conditions have been achieved and if it is probable that a significant revenue reversal would not occur before recognizing the associated revenue. We determined that these milestone payments are not within our control or the licensee's control, such as regulatory approvals, and are not considered probable of being achieved until those approvals are received. Accordingly, we have fully constrained the $26.5 million of event-based milestone payments until such time that it is probable that significant revenue reversal would not occur. The sales-based milestone payments and other royalty-based payments are based on a level of sales for which the license is deemed to be the predominant item to which the royalties relate. We will recognize revenue for these payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, we have not recognized any sales-based or royalty revenue resulting from this licensing arrangement.

Under this arrangement, we recognized $3.0 million of revenue during the year ended December 31, 2020, which amount related solely to fixed consideration. We do not have any contract assets or contract liabilities as a result of this transaction.

Foundation Revenues: Foundation revenues relate to a collaborative agreement between nine Sanfilippo foundations to provide up to approximately $13.9 million of grants to Abeona in installments for the advancement of our clinical stage gene therapies for MPS IIIA and MPS IIIB, subject to the achievement of certain milestones. We have assessed the ASC 606-10-25-27 criteria used to determine whether foundation revenue should be recognized over time and determined that our performance does not create an asset with an alternative use to the foundations and we have an enforceable right to payment for performance completed to date. We determined that the input method based on costs incurred in accordance with ASC 606-10-55-20 would be the most appropriate method for measuring progress. As a result, we have concluded that cash received upfront from the foundations should be deferred on the balance sheet until the costs of the activities as outlined in the manufacturing and clinical work plan are incurred by installment as outlined in the agreement with the foundations. Effectively, this matches the revenue up to the costs incurred by installment. Should the aggregate cash received exceed the costs incurred by installment, the excess of aggregate cash over costs will be deferred. We have foundation revenue of $0.3 million recorded as deferred revenue on the balance sheet as of December 31, 2020 and 2019. In 2020 and 2019, we did not record any foundation revenues since no milestones were achieved.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation Expense

We account for share-based compensation expense in accordance with ASC 718, *Stock Based Compensation*. We have two share-based compensation plans under which incentive and qualified stock options and restricted shares may be granted to employees, directors, and consultants. We measure the cost of the employee/director/consultant services received in exchange for an award of equity instruments based on the fair value for employees and directors and vesting date fair value of the award for consultants. We use the Black-Scholes option pricing model to determine the fair value of options as of the grant date and the Hull White I lattice model as of any option repricing dates. The models used to determine the fair value of options includes assumptions for expected volatility, risk-free interest rate, dividend yield and estimated expected term. We use the closing price of our common stock as quoted on Nasdaq to determine the fair value of restricted stock. We account for forfeitures as they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise.

Stock option-based compensation expense recognized for the years ended December 31, 2020 and 2019 was approximately $5.9 million and $7.3 million, respectively. Restricted stock-based compensation expense recognized for the years ended December 31, 2020 and 2019 was approximately $2.3 million and $0.9 million, respectively.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Financial statements required by this Item are incorporated in this Annual Report Form 10-K on pages F-1 through F-21 hereto. Reference is made to Item 15 of this Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")), as of the end of the period covered by this Annual Report on Form 10-K. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of such date, our disclosure controls and procedures were effective.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements. Under the supervision and with the participation of management, including our principal executive and financial officers, we assessed our internal control over financial reporting as of December 31, 2020, based on criteria for effective internal control over financial reporting established in Internal Control — Integrated Framework (2013), issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Our management's assessment of the effectiveness of our internal control over financial reporting included testing and evaluating the design and operating effectiveness of our internal controls. In our management's opinion, we have maintained effective internal control over financial reporting as of December 31, 2020, based on criteria established in the COSO 2013 framework.

Because we are a non-accelerated filer and smaller reporting company, Whitley Penn LLP, our independent registered public accounting firm, is not required to attest to or issue a report on the effectiveness of our internal control over financial reporting.

Inherent Limitations of Internal Controls

Our management, including our principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures or our internal controls will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a 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 management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, during the fourth quarter of 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Directors and Reports of Beneficial Ownership. The information required by this Item is incorporated herein by reference from the information to be contained in our 2021 Proxy Statement to be filed with the SEC within 120 days after December 31, 2020 in connection with the solicitation of proxies for our 2021 Annual Meeting of Stockholders (the "2021 Proxy Statement").

Code of Ethics. We have adopted a Code of Business Conduct and Ethics (the "Code") that applies to all of our employees (including executive officers) and directors. The Code is available on our website at www.abeonatherapeutics.com under the heading "Investors & Media—Corporate Governance—Governance—Governance Documents." We intend to satisfy the disclosure requirement regarding any waiver of a provision of the Code applicable to any executive officer or director, by posting such information on such website. We shall provide to any person without charge, upon request, a copy of the Code. Any such request must be made in writing to Abeona Therapeutics Inc., c/o Investor Relations, 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019.

Our corporate governance guidelines and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee of the Board of Directors are available on our website at www.abeonatherapeutics.com under the heading "Investors & Media—Corporate Governance—Governance—Governance Documents." We shall provide to any person without charge, upon request, a copy of any of the foregoing materials. Any such request must be made in writing to Abeona Therapeutics Inc., c/o Investor Relations, 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is contained in the 2021 Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item is contained in the 2021 Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

The information required by this Item is contained in the 2021 Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item is contained in the 2021 Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

	Page
a. Financial Statements. The following financial statements are submitted as part of this report:	
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets at December 31, 2020 and 2019	F-2
Consolidated Statements of Operations and Comprehensive Loss for 2020 and 2019	F-3
Consolidated Statements of Stockholders' Equity for 2020 and 2019	F-4
Consolidated Statements of Cash Flows for 2020 and 2019	F-5
Notes to Consolidated Financial Statements	F-6

b. Exhibits

Exhibit Number	Description of Document
3.1	Restated Certificate of Incorporation of Abeona Therapeutics Inc. (incorporated by reference to Exhibit 3.1 of our Form 10-Q for the quarter ended March 31, 2019)
3.2	Amended and Restated Bylaws of Abeona Therapeutics Inc. (incorporated by reference to Exhibit 3.1 of our Form 8-K filed on May 21, 2020)
4.1*	2015 Equity Incentive Plan (incorporated by reference to Exhibit 4.1 to our Form S-8 filed May 11, 2015)
4.2*	2015 Equity Incentive Plan Amendment (incorporated by reference to our Definitive Proxy Statement on Schedule 14A filed on April 4, 2016)
4.3	Description of Capital Stock of Abeona Therapeutics Inc. (incorporated by reference to Exhibit 4.4 of our Form 10-K for the year ended December 31, 2019)
10.1*	401(k) Plan (incorporated by reference to Exhibit 10.20 of our Form 10-K for the year ended December 31, 1999)
10.2*	2005 Equity Incentive Plan (incorporated by reference to Exhibit 1 of our Proxy Statement filed on April 18, 2005)
10.3	Director Designation Agreement dated November 15, 2007, between the Company and SCO Capital Partners LLC (incorporated by reference to Exhibit 10.26 of our Form S-1 filed on March 11, 2008)
10.4	Agreement and Plan of Merger, dated May 5, 2015, by and among the Company, PlasmaTech Merger Sub Inc., Abeona Therapeutics LLC and Paul A. Hawkins, in his capacity as Member Representative (incorporated by reference to Exhibit 10.1 to our Form 10-Q for the quarter ended June 30, 2015)
10.5	Form of Indemnification Agreement, between the Company and directors and officers of the Company (incorporated by reference to Exhibit 10.1 to our Form 8-K filed on October 16, 2020)
10.6*	Letter Agreement, dated October 26, 2020, between the Company and Michael Amoroso (incorporated by reference to Exhibit 10.1 of our Form 8-K filed on October 30, 2020)
10.7*	Offer Letter, effective October 19, 2018, by and between the Company and Edward Carr (incorporated by reference to Exhibit 10.1 of Form 8-K filed on November 9, 2018)
10.8*	Letter Agreement, dated September 12, 2019, amending Offer Letter between the Company and Edward Carr, dated November 8, 2018 (incorporated by reference to Exhibit 10.3 of our Form 10-Q for the quarter ended September 30, 2019)
10.9*	Offer Letter, dated June 18, 2020, between the Company and Edward Carr (incorporated by reference to Exhibit 10.1 of our Form 8-K filed on June 23, 2020)

10.10	Open Market Sale Agreement, dated August 17, 2018, by and between the Company and Jefferies LLC (incorporated by reference to Exhibit 1.1 of Form 8-K filed on August 20, 2018)
10.11+	License Agreement, dated November 4, 2018, between the Company and REGENXBIO Inc. (incorporated by reference to Exhibit 10.18 of our Form 10-K for the year ended December 31, 2018)
10.12†	First Amendment to License Agreement, dated November 4, 2019, between the Company and REGENXBIO Inc. (incorporated by reference to Exhibit 10.4 of our Form 10-Q for the quarter ended September 30, 2019)
21	Subsidiaries of the registrant
23.1	Consent of Whitley Penn LLP
31.1	Principal Executive Officer Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Principal Financial Officer Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32	Principal Executive Officer Certification and Principal Financial Officer Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101	The following materials from Abeona's Annual Report on Form 10-K for the year ended December 31, 2020, formatted in Inline XBRL (Extensible Business Reporting Language): (i) Consolidated Balance Sheets at December 31, 2020 and 2019, (ii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2020 and 2019, (iii) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2020 and 2019, (iv) Condensed Consolidated Statements of Cash Flows for the years ended December 31, 2020 and 2019, and (v) Notes to Condensed Consolidated Financial Statements.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and included in Exhibit 101).

* Management contract or compensatory plan required to be filed as an Exhibit to this Form pursuant to Item 15c of the report.
+ Portions of this exhibit were omitted and filed separately with the SEC pursuant to a request for confidential treatment.
† Certain identified information has been excluded from this exhibit pursuant to Item 601(b)(10)(iv) of Regulation S-K.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

ABEONA THERAPEUTICS INC.

Date: March 24, 2021

By: */s/ Michael Amoroso*
Michael Amoroso
President, Chief Executive Officer and Director
Principal Executive Officer

Date: March 24, 2021

By: */s/ Edward Carr*
Edward Carr
Chief Accounting Officer
Principal Financial and Accounting Officer

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

Date: March 24, 2021

By: */s/ Michael Amoroso*
Michael Amoroso
President, Chief Executive Officer and Director
Principal Executive Officer

Date: March 24, 2021

By: */s/ Edward Carr*
Edward Carr
Chief Accounting Officer
Principal Financial and Accounting Officer

Date: March 24, 2021

By: */s/ Paul Mann*
Paul Mann, Director

Date: March 24, 2021

By: *s/ Steven H. Rouhandeh*
Steven H. Rouhandeh, Director
Chairman of the Board

Date: March 24, 2021

By: */s/ Christine Silverstein*
Christine Silverstein, Director

Date: March 24, 2021

By: */s/ Todd Wider*
Todd Wider, Director

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders
Abeona Therapeutics Inc. and Subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Abeona Therapeutics and Subsidiaries (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of their operations and their cash flows for the years then ended, 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 these financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting, but not for the purpose of expressing an opinion on the effectiveness of the entity'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.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ WHITLEY PENN LLP

We have served as the Company's auditor since 2006.

Plano, Texas
March 24, 2021

Abeona Therapeutics Inc. and Subsidiaries
CONSOLIDATED BALANCE SHEETS

	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 12,596,000	$ 129,258,000
Short-term investments	82,438,000	-
Prepaid expenses and other current assets	2,708,000	3,132,000
Total current assets	97,742,000	132,390,000
Property and equipment, net	11,322,000	13,157,000
Right-of-use lease assets	7,032,000	8,047,000
Licensed technology, net	1,500,000	36,178,000
Goodwill	32,466,000	32,466,000
Other assets and restricted cash	1,136,000	1,144,000
Total assets	$ 151,198,000	$ 223,382,000
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,695,000	$ 3,763,000
Accrued expenses	3,410,000	5,543,000
Current portion of lease liability	1,713,000	1,699,000
Current portion of loan payable	330,000	-
Payable to licensor	31,515,000	27,400,000
Deferred revenue	296,000	296,000
Total current liabilities	41,959,000	38,701,000
Loan payable	1,428,000	-
Long-term lease liabilities	5,260,000	6,251,000
Total liabilities	48,647,000	44,952,000
Commitments and contingencies		
Stockholders' equity:		
Common stock - $0.01 par value; authorized 200,000,000 shares; issued and outstanding 96,131,678 at December 31, 2020; issued and outstanding 83,622,135 at December 31, 2019;	961,000	836,000
Additional paid-in capital	672,304,000	664,064,000
Accumulated deficit	(570,704,000)	(486,470,000)
Accumulated other comprehensive loss	(10,000)	-
Total stockholders' equity	102,551,000	178,430,000
Total liabilities and stockholders' equity	$ 151,198,000	$ 223,382,000

The accompanying notes are an integral part of these consolidated statements.

Abeona Therapeutics Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	For the years ended December 31,	
	2020	**2019**
Revenues:		
License and other revenues	$ 10,000,000	$ -
Total revenues	10,000,000	-
Expenses:		
Research and development	30,139,000	48,566,000
General and administrative	23,779,000	20,705,000
Depreciation and amortization	4,586,000	7,819,000
Licensed technology impairment charge	32,916,000	-
Total expenses	91,420,000	77,090,000
Loss from operations	(81,420,000)	(77,090,000)
Interest and miscellaneous income	1,301,000	1,208,000
Interest and other expense	(4,115,000)	(400,000)
Net loss	$ (84,234,000)	$ (76,282,000)
Basic and diluted loss per common share	$ (0.91)	$ (1.51)
Weighted average number of common shares outstanding – basic and diluted	92,663,574	50,354,596
Other comprehensive loss:		
Change in unrealized losses related to available-for-sale debt securities	(10,000)	-
Comprehensive loss	$ (84,244,000)	$ (76,282,000)

The accompanying notes are an integral part of these consolidated statements.

Abeona Therapeutics Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	Equity
Balance, December 31, 2018	47,944,486	$ 479,000	$ 543,754,000	$ (410,188,000)	$ -	$ 134,045,000
Stock option-based compensation expense	-	-	7,338,000	-	-	7,338,000
Restricted stock-based compensation expense	-	-	899,000	-	-	899,000
Issuance of common stock and pre-funded warrants in connection with public offering, net of offering costs	32,382,945	324,000	95,648,000	-	-	95,972,000
Issuance of common stock under open market sale agreement	3,086,950	31,000	16,930,000	-	-	16,961,000
Issuance of common stock in connection with the exercise of stock options	303,129	3,000	966,000	-	-	969,000
Issuance of common stock in connection with restricted share awards, net of cancellations	354,625	4,000	(4,000)	-	-	-
Shares returned in connection with arbitration ruling on licensing agreement	(450,000)	(5,000)	(1,467,000)	-	-	(1,472,000)
Net loss	-	-	-	(76,282,000)	-	(76,282,000)
Balance, December 31, 2019	83,622,135	$ 836,000	$ 664,064,000	$ (486,470,000)	$ -	$ 178,430,000
Stock option-based compensation expense	-	-	5,853,000	-	-	5,853,000
Restricted stock-based compensation expense	-	-	2,334,000	-	-	2,334,000
Issuance of common stock in connection with the exercise of stock options	77,560	1,000	176,000	-	-	177,000
Issuance of common stock in connection with restricted share awards, net of cancellations	3,414,928	34,000	(34,000)	-	-	-
Issuance of common stock in connection with the exercise of pre-funded warrants	9,017,055	90,000	(89,000)	-	-	1,000
Net loss	-	-	-	(84,234,000)	-	(84,234,000)
Other comprehensive loss	-	-	-	-	(10,000)	(10,000)
Balance, December 31, 2020	96,131,678	$ 961,000	$ 672,304,000	$ (570,704,000)	$ (10,000)	$ 102,551,000

The accompanying notes are an integral part of these consolidated statements.

Abeona Therapeutics Inc. and Subsidiaries
CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the years ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (84,234,000)	$ (76,282,000)
Adjustments to reconcile net loss to cash used in operating activities:		
Non-cash licensed technology impairment charge	32,916,000	-
Depreciation and amortization	4,586,000	7,819,000
Stock option-based compensation expense	5,853,000	7,338,000
Restricted stock-based compensation expense	2,334,000	899,000
Non-cash interest expense	600,000	-
Accretion and interest on short-term investments	(70,000)	(266,000)
Accretion of right-of-use lease assets	1,015,000	858,000
Other	347,000	367,000
Change in operating assets and liabilities:		
Receivables	-	81,000
Prepaid expenses and other current assets	424,000	670,000
Other assets	(127,000)	3,000
Accounts payable, accrued expenses and lease liabilities	(2,178,000)	(1,707,000)
Change in payable to licensor	3,515,000	(2,600,000)
Net cash used in operating activities	(35,019,000)	(62,820,000)
Cash flows from investing activities:		
Capital expenditures	(1,336,000)	(6,309,000)
Acquisition of licensed technology	-	(199,000)
Purchases of short-term investments	(170,472,000)	-
Proceeds from maturities of short-term investments	88,094,000	66,484,000
Net cash (used in)/provided by investing activities	(83,714,000)	59,976,000
Cash flows from financing activities:		
Proceeds from loan payable	1,758,000	-
Proceeds from issuance of common stock and pre-funded warrants in public offering, net of offering costs	1,000	95,972,000
Proceeds from open market sales of common stock	-	16,961,000
Proceeds from exercise of stock options	177,000	969,000
Net cash provided by financing activities	1,936,000	113,902,000
Net (decrease)/increase in cash, cash equivalents and restricted cash	(116,797,000)	111,058,000
Cash, cash equivalents and restricted cash at beginning of year	130,368,000	19,310,000
Cash, cash equivalents and restricted cash at end of year	$ 13,571,000	$ 130,368,000
Supplemental cash flow information:		
Cash and cash equivalents	$ 12,596,000	$ 129,258,000
Restricted cash	975,000	1,110,000
Total cash, cash equivalents and restricted cash	$ 13,571,000	$ 130,368,000
Shares returned in connection with arbitration ruling on licensing agreement	$ -	$ 1,472,000
Cash paid for interest	$ -	$ -
Cash paid for taxes	$ -	$ -

The accompanying notes are an integral part of these consolidated statements.

NOTE 1 - NATURE OF OPERATIONS AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Nature of Operations

Abeona Therapeutics Inc. (together with our subsidiaries, "we," "our," "Abeona" or the "Company"), a Delaware corporation, is a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases. Our lead clinical programs consist of: (i) EB-101, an autologous, gene-corrected cell therapy for recessive dystrophic epidermolysis bullosa ("RDEB"), (ii) ABO-102, an adeno-associated virus ("AAV")-based gene therapy for Sanfilippo syndrome type A ("MPS IIIA"), and (iii) ABO-101, an AAV-based gene therapy for Sanfilippo syndrome type B ("MPS IIIB"). We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases and next-generation AAV-based gene therapies using the novel AIM™ capsid platform that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs.

A summary of the significant accounting policies applied in the preparation of the accompanying consolidated financial statements follows:

Principles of Consolidation

The consolidated financial statements include the financial statements of Abeona Therapeutics Inc. and our wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Uses and Sources of Liquidity

The financial statements have been prepared on the going concern basis, which assumes the Company will have sufficient cash to pay its operating expenses, as and when they become payable, for a period of at least 12 months from the date the financial report was issued.

As of December 31, 2020, we had cash, cash equivalents and short-term investments of $95.0 million and net assets of $102.6 million. For the year ended December 31, 2020, we had cash outflows from operations of $35.0 million. We have not generated significant product revenues and have not achieved profitable operations. There is no assurance that profitable operations will ever be achieved, and, if achieved, could be sustained on a continuing basis. In addition, development activities, clinical and nonclinical testing, and commercialization of our products will require significant additional financing.

We are subject to a number of risks similar to other life science companies, including, but not limited to, risks related to the successful discovery and development of product candidates, obtaining the necessary regulatory approval to market our product candidates, raising additional capital to continue to fund our operations, development of competing drugs and therapies, protection of proprietary technology and market acceptance of our products. As a result of these and other risks and the related uncertainties, there can be no assurance of our future success.

Based upon our current operating plans, we believe that we have sufficient resources to fund operations through at least the next 12 months with our existing cash, cash equivalents and short-term investments. We will need to secure additional funding in the future, to carry out all our planned research and development activities. If we are unable to obtain additional financing or generate license or product revenue, the lack of liquidity and sufficient capital resources could have a material adverse effect on our future prospects.

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") requires management to make estimates and assumptions that affect the reported amount of assets and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reported period. Actual results could differ from these estimates and assumptions.

Cash and Cash Equivalents

We consider all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. We maintain deposits primarily in financial institutions, which may at times exceed amounts covered by insurance provided by the U.S. Federal Deposit Insurance Corporation ("FDIC"). We have not experienced any losses related to amounts in excess of FDIC limits.

Short-term Investments

Short-term investments consist of investments in U.S. government, U.S. agency and U.S. treasury securities. We determine the appropriate classification of the securities at the time they are acquired and evaluate the appropriateness of such classifications at each balance sheet date. We classify our short-term investments as available-for-sale pursuant to Accounting Standards Codification ("ASC") 320, *Investments – Debt and Equity Securities*. Investments classified as current have maturities of less than one year. We review our short-term investments for other-than-temporary impairment whenever the fair value of a marketable security is less than the amortized cost and evidence indicates that a short-term investment's carrying amount is not recoverable within a reasonable period of time.

Property and Equipment

Property and equipment are recorded at cost. Depreciation is provided using the straight-line method over estimated useful lives ranging from three to seven years for equipment and five to ten years for leasehold improvements. Expenditures for major renewals and betterments that extend the useful lives are capitalized. Expenditures for normal maintenance and repairs are expensed as incurred. The cost of assets sold or abandoned, and the related accumulated depreciation are eliminated from the accounts and any gains or losses are recognized in the accompanying consolidated statements of operations of the respective period.

Leases

We account for leases in accordance with ASC 842, *Leases*. Right-of-use lease assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. The measurement of lease liabilities is based on the present value of future lease payments over the lease term. As our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. The right-of-use asset is based on the measurement of the lease liability and includes any lease payments made prior to or on lease commencement and excludes lease incentives and initial direct costs incurred, as applicable. Rent expense for our operating leases is recognized on a straight-line basis over the lease term. We do not have any leases classified as finance leases.

Our leases do not have significant rent escalation, holidays, concessions, material residual value guarantees, material restrictive covenants or contingent rent provisions. Our leases include both lease (e.g., fixed payments including rent, taxes, and insurance costs) and non-lease components (e.g., common-area or other maintenance costs), which are accounted for as a single lease component as we have elected the practical expedient to group lease and non-lease components for all leases.

Most leases include one or more options to renew. The exercise of lease renewal options is typically at our sole discretion; therefore, the majority of renewals to extend the lease terms are not included in our right-of-use assets and lease liabilities as they are not reasonably certain of exercise. We regularly evaluate the renewal options and when they are reasonably certain of exercise, we include the renewal period in our lease term.

Additional information and disclosures required under ASC 842 are included in Note 12.

Licensed Technology

We have entered into agreements to license the rights to certain technologies. We recorded the purchase price paid for the license, which represents fair value, on our consolidated balance sheet. We maintain licensed technology on our consolidated balance sheet until either the licensed technology agreement underlying it is completed or the asset becomes impaired. When we determine that an asset has become impaired or we abandon a project, we write down the carrying value of the related intangible asset to its fair value and take an impairment charge in the period in which the impairment occurs. Licensed technology is amortized over the life of the patent or the agreement and periodically reviewed for impairment.

We test our intangible assets for impairment on an annual basis, or more frequently if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding our drug candidate or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate or new information regarding potential sales for the drug. In connection with each annual impairment assessment and any interim impairment assessment, we compare the fair value of the asset as of the date of the assessment with the carrying value of the asset on our consolidated balance sheet.

We considered the status of our discussions with REGENXBIO in March 2020 as a potential indicator of impairment in accordance with ASC 360-10-35-21. Our impairment test indicated that the carrying value of the license agreement exceeded its fair value and we recorded a $32.9 million non-cash impairment charge in 2020. We did not recognize any impairment charges to related licensed technology in 2019.

Goodwill

As of December 31, 2020 and 2019, goodwill of $32.5 million was recorded on the Company's consolidated balance sheet. In accordance with ASC 350, *Intangibles — Goodwill and Other,* goodwill is tested annually for impairment and whenever changes in circumstances occur that would indicate impairment. The Company did not recognize any impairment charges related to goodwill in 2020 or 2019.

Restricted Cash

Restricted cash is recorded within other assets and restricted cash in the accompanying consolidated balance sheets and is included as a component of cash, cash equivalents and restricted cash on our consolidated statements of cash flows.

Segments

The Company operates in a single segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources.

Revenue Recognition

We account for contracts with customers in accordance with ASC 606, *Revenue from Contracts with Customers*. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

Additional information and disclosures required under ASC 606 are included in Note 8.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses include, but are not limited to, payroll and personnel expense, lab supplies, preclinical, development cost, clinical trial expense, manufacturing, and consulting. The cost of materials and equipment or facilities that are acquired for research and development activities and that have alternative future uses are capitalized when acquired.

General and Administrative Expenses

General and administrative expenses primarily consist of personnel, contract personnel, personnel-related expenses to support our administrative and operating activities, facility costs and professional expenses (i.e., legal expenses) and investor relations fees.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the consolidated financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance is provided for deferred tax assets to the extent their realization is in doubt.

We account for uncertain income tax positions in accordance with ASC 740, *Income Taxes*. Interest costs and penalties related to income taxes are classified as interest expense and general and administrative costs, respectively, in our consolidated financial statements. For 2020 and 2019, we did not recognize any uncertain tax positions, interest or penalty expense related to income taxes. It is not reasonably likely for the amounts of unrecognized tax benefits to significantly increase or decrease within the next 12 months. We file U.S. federal and state income tax returns as necessary. The federal return generally has a three-year statute of limitations and most states have a four-year statute of limitations; however, the taxing authorities are allowed to review the tax year in which the net operating loss was generated when the loss is utilized on a tax return. We currently do not have any open income tax audits.

Loss Per Common Share

We have presented basic and diluted loss per common share on the statement of operations and comprehensive loss. Basic and diluted net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock and shares underlying "pre-funded" warrants outstanding during the period. The "pre-funded" warrants were included in the computation of basic net loss per share as the exercise price was negligible and the warrants were fully vested and exercisable. In October 2020, all of the 9,017,055 "pre-funded" warrants were exercised and converted into shares of common stock.

We do not include the potential impact of dilutive securities in diluted net loss per share, as the impact of these items is anti-dilutive. Potential dilutive securities result from outstanding stock options, restricted stock and "non-pre-funded" warrants. We did not include the following potentially dilutive securities in the computation of diluted net loss per common share during the periods presented:

	For the years ended December 31,	
	2020	**2019**
Warrants	-	70,000
Restricted stock	2,952,499	354,625
Stock options	5,685,539	6,055,395
Total	8,638,038	6,480,020

Stock-Based Compensation

We account for stock-based compensation expense in accordance with ASC 718, *Stock Based Compensation*. We measure the cost of the employee/director/consultant services received in exchange for an award of equity instruments based on the grant date fair value for the employees and directors and vesting date fair value for consultants of the award. We use the Black-Scholes option pricing model to determine the fair value of options on the grant date which includes assumptions for expected volatility, risk-free interest rate, dividend yield and estimated expected term. We use the closing price of our common stock as quoted on the Nasdaq to determine the fair value of restricted stock. We account for forfeitures as they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise.

The fair value of modifications to share-based awards are determined using Hull White I lattice model which includes assumptions for expected volatility, risk-free interest rate, dividend yield and performance period. If a share-based compensation award is modified after the grant date, incremental compensation expense, if any, is recognized in an amount equal to the excess of the fair value of the modified award over the fair value of the original award immediately before the modification. Incremental compensation expense for vested awards is recognized immediately. For unvested awards, the sum of the incremental compensation expense and the remaining unrecognized compensation expense for the original award on the modification date is recognized over the modified service period.

The following table summarizes stock option-based option compensation for 2020 and 2019, which was allocated as follows:

	For the years ended December 31,	
	2020	**2019**
Research and development	$ 3,126,000	$ 3,932,000
General and administrative	2,727,000	3,406,000
Stock option-based compensation expense included in operating expense	5,853,000	7,338,000
Total stock option-based compensation expense	5,853,000	7,338,000
Tax benefit	-	-
Stock option-based compensation expense, net of tax	$ 5,853,000	$ 7,338,000

The following table summarizes restricted stock-based compensation for 2020 and 2019, which was allocated as follows:

	For the years ended December 31,	
	2020	2019
Research and development	$ 957,000	$ 454,000
General and administrative	1,377,000	445,000
Restricted stock-based compensation expense included in operating expense	2,334,000	899,000
Total restricted stock-based compensation expense	2,334,000	899,000
Tax benefit	-	-
Restricted stock-based compensation expense, net of tax	$ 2,334,000	$ 899,000

Additional information and disclosures required under ASC 718 are included in Note 9.

NOTE 2 – SHORT-TERM INVESTMENTS

The following table summarizes the available-for-sale investments held as of December 31, 2020. There were no available-for-sale investments as of December 31, 2019.

Description	Fair value
U.S. government and agency securities and treasuries	$ 82,438,000

The amortized cost of the available-for-sale investments, which is adjusted for amortization of premiums and accretion of discounts to maturity, was $82,448,000 as of December 31, 2020. There were no significant realized gains or losses recognized on the sale or maturity of available-for-sale investments during the years ended December 31, 2020 or 2019.

NOTE 3 - PROPERTY AND EQUIPMENT

Property and equipment consist of the following:

	December 31, 2020	December 31, 2019
Laboratory equipment	$ 8,160,000	$ 7,031,000
Furniture and office equipment	1,818,000	1,710,000
Leasehold improvements	8,602,000	8,573,000
Construction work-in-progress	71,000	-
	18,651,000	17,314,000
Less: accumulated depreciation and amortization	7,329,000	4,157,000
Property and equipment, net	$ 11,322,000	$ 13,157,000

Depreciation and amortization on property and equipment was $3.2 million and $2.6 million for 2020 and 2019, respectively.

NOTE 4 – LICENSED TECHNOLOGY

On November 4, 2018, we entered into a license agreement with REGENXBIO Inc. ("REGENXBIO") to obtain rights to an exclusive worldwide license (subject to certain non-exclusive rights previously granted for MPS IIIA), with rights to sublicense, to REGENXBIO's NAV AAV9 vector for gene therapies for treating MPS IIIA, MPS IIIB, CLN1 Disease and CLN3 Disease. Consideration for the rights granted under the original agreement included fees totaling $180 million and a running royalty on net sales, including: (i) an initial fee of $20 million, $10 million of which was due to REGENXBIO shortly after the effective date of the agreement, and $10 million of which was to be due on the first anniversary of the effective date of the agreement in November 2019, (ii) annual fees totaling up to $100 million, payable in $20 million annual installments beginning on the second anniversary of the effective date (the first of which was to remain payable if the agreement were terminated before the second anniversary in November 2020), (iii) sales milestone payments totaling $60 million, and (iv) royalties payable in the low double digits to low teens on net sales of products covered under the agreement. The license was being amortized over the life of the patent of eight years. On November 1, 2019, we entered into an amendment of the original license agreement. The amended agreement replaced the $10 million payment due on November 4, 2019 with a $3 million payment due on November 4, 2019 and an additional $8 million payment (which included $1 million of interest) that would have been due no later than April 1, 2020. That $8 million payment had been scheduled to be paid by April 1, 2020 and the $20 million that had been due to be paid on November 4, 2020, and both were recorded as payable to licensor on the consolidated balance sheet. The Company has disputed that it is responsible for the $8 million and $20 million payments, and those payments are the subject of a current arbitration between the Company and REGENXBIO.

Prior to the April 1, 2020 deadline, we engaged REGENXBIO in discussions in an attempt to renegotiate the financial terms of the agreement, but we were unable to reach a mutual understanding that we believed would have been favorable for the Company or our programs, and we did not make the $8 million payment due by April 1, 2020. On April 17, 2020, REGENXBIO sent us a written demand for the $8 million fee, payable within a 15-day cure period after receipt of the demand letter. The license terminated on May 2, 2020, when the 15-day period expired. There were no penalties for early termination of the license. On May 25, 2020, we filed an arbitration claim with the American Arbitration Association ("AAA") alleging that REGENXBIO materially breached the license agreement prior to termination and seeking, among other things, a declaration that as a result of REGENXBIO's material breach, we are not responsible for payments totaling $28 million (which would otherwise have been due in 2020) plus accrued interest ($3.5 million as of December 31, 2020). REGENXBIO disputes our arbitration claim and has filed a counterclaim seeking payment of the $28 million plus interest, which REGENXBIO argues remains due. An arbitration hearing before a tribunal of three AAA arbitrators was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021. Additional information is included in Note 12.

We considered the status of our discussions with REGENXBIO in March 2020 as a potential indicator of impairment in accordance with ASC 360-10-35-21. Our impairment test indicated that the carrying value of the license agreement exceeded its fair value and we recorded a $32.9 million non-cash impairment charge.

On May 15, 2015, we acquired Abeona Therapeutics LLC, which had an exclusive license through Nationwide Children's Hospital to the AB-101 and AB-102 patent portfolios for developing treatments for patients with Sanfilippo Syndrome Type A and Type B. The license is amortized over the life of the license of 20 years.

Licensed technology consists of the following:

	December 31, 2020	December 31, 2019
Licensed technology	$ 2,156,000	$ 42,606,000
Less accumulated amortization	656,000	6,428,000
Licensed technology, net	$ 1,500,000	$ 36,178,000

The aggregate estimated amortization expense for intangible assets remaining as of December 31, 2020 is as follows:

2021	$ 117,000
2022	117,000
2023	117,000
2024	117,000
2025	117,000
Thereafter	915,000
Total	$ 1,500,000

Amortization on licensed technology was $1.4 million and $5.2 million for the years ended December 31, 2020 and 2019, respectively.

NOTE 5 – LOAN PAYABLE

On May 2, 2020, we received loan proceeds in the amount of approximately $1.8 million (the "PPP Loan") under the Paycheck Protection Program ("PPP"). The PPP was established under the Coronavirus Aid, Relief and Economic Security Act, as amended ("CARES Act") and is administered by the U.S. Small Business Administration ("SBA"). Under the terms of the CARES Act, PPP loan recipients can apply for loan forgiveness. The potential loan forgiveness for all or a portion of PPP loans is determined, subject to limitations, based on the use of loan proceeds over the 24 weeks after the loan proceeds are disbursed. The amount of loan forgiveness will be reduced if PPP loan recipients terminate employees or reduce salaries during the covered period. The unforgiven portion of our PPP Loan, if any, is payable over two years at an interest rate of 1%, with a deferral of principal and interest payments to either (i) the date that the SBA remits the borrower's loan forgiveness amount to the lender or (ii) if the borrower does not apply for forgiveness, 10 months after the end of the borrower's loan forgiveness covered period. We believe that we have used the proceeds from our PPP Loan for purposes consistent with the PPP. While we currently believe that our use of the loan proceeds will meet the conditions for forgiveness of our PPP Loan, there can be no assurance that forgiveness for any portion of the PPP Loan will be obtained.

NOTE 6 - FAIR VALUE MEASUREMENTS

We calculate the fair value of our assets and liabilities that qualify as financial instruments and include additional information in the notes to the consolidated financial statements when the fair value is different than the carrying value of these financial instruments. The estimated fair value of prepaid expenses and other current assets, other assets, accounts payable, accrued expenses, loan payable, payable to licensor and deferred revenue approximate their carrying amounts due to the relatively short maturity of these instruments.

U.S. GAAP defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. This guidance establishes a three-level fair value hierarchy that prioritizes the inputs used to measure fair value. The hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows:

- Level 1 – Quoted prices in active markets for identical assets or liabilities.
- Level 2 – Observable inputs other than quoted prices included in Level 1, such as quoted prices for similar assets and liabilities in active markets; quoted prices for identical or similar assets and liabilities in markets that are not active; or other inputs that are observable or can be corroborated by observable market data.
- Level 3 – Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets and liabilities. This includes certain pricing models, discounted cash flow methodologies and similar valuation techniques that use significant unobservable inputs.

The guidance requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

We have segregated all financial assets and liabilities that are measured at fair value on a recurring basis (at least annually) into the most appropriate level within the fair value hierarchy based on the inputs used to determine the fair value at the measurement date in the table below.

Financial assets and liabilities measured at fair value on a recurring and non-recurring basis as of December 31, 2020 and 2019 are summarized below:

Description	December 31, 2020	Level 1	Level 2	Level 3	Total Gains/(Losses)
Recurring					
Assets:					
Short-term investments	$ 82,438,000	$ -	$ 82,438,000	$ -	$ -
Non-recurring					
Assets:					
Licensed technology, net	$ 1,500,000	$ -	$ -	$ 1,500,000	$ (32,916,000)
Goodwill	32,466,000	-	-	32,466,000	-

Description	December 31, 2019	Level 1	Level 2	Level 3	Total Gains/(Losses)
Recurring					
Assets:					
Short-term investments	$ -	$ -	$ -	$ -	$ -
Non-recurring					
Assets:					
Licensed technology, net	$ 36,178,000	$ -	$ -	$ 36,178,000	$ (367,000)
Goodwill	32,466,000	-	-	32,466,000	-

NOTE 7 – STOCKHOLDERS' EQUITY

2019 Public Offering of Common Stock and "Pre-Funded" Warrants

On December 24, 2019, we closed an underwritten public offering of 32,382,945 shares of common stock at a public offering price of $2.50 per share. In addition, as part of the offering, we sold "pre-funded" warrants to purchase up to an aggregate of 9,017,055 shares of common stock at a purchase price of $2.4999 per pre-funded warrant, which equals the public offering price per share of the common stock less the $0.0001 per share exercise price of each pre-funded warrant. The gross proceeds to the Company were approximately $103.5 million, before deducting the underwriting discounts and commissions and estimated offering expenses payable by the Company.

In October 2020, all of the 9,017,055 "pre-funded" warrants were exercised and converted into 9,017,055 shares of common stock. We received a negligible amount of cash from the exercise of these pre-funded warrants during 2020.

"Non-Pre-Funded" Warrants

"Non-pre-funded" warrants to purchase a total of 70,000 shares of common stock were outstanding as of December 31, 2019. These "non-pre-funded" warrants expired unexercised during 2020. We did not receive cash from the exercise of "non-pre-funded" warrants during 2020 or 2019.

NOTE 8 – REVENUE FROM CONTRACTS WITH CUSTOMERS

Sublicense and Inventory Purchase Agreements Relating to CLN1 Disease: In August 2020, we entered into sublicense and inventory purchase agreements with Taysha Gene Therapies ("Taysha") relating to a potential gene therapy for CLN1 disease. Under the sublicense agreement, Taysha received worldwide exclusive rights to intellectual property and know-how relating to the research, development, and manufacture of the potential gene therapy, which we had referred to as ABO-202. Under the inventory purchase agreement, we sold to Taysha certain inventory and other items related to ABO-202. We assessed these contracts at contract inception and determined that, under ASC 606, the two contracts would be combined and accounted for as a single contract, with a single performance obligation. We assessed the nature of the promised license to determine whether the license has significant stand-alone functionality and evaluated whether such functionality can be retained without ongoing activities by us and determined that the license has significant stand-alone functionality. Furthermore, we have no ongoing activities associated with the license to support or maintain the license's utility. Based on this, we determined that the pattern of transfer of control of the license to Taysha was at a point in time.

The transaction price of the contract includes (i) $7.0 million of fixed consideration, (ii) up to $26.0 million of variable consideration in the form of event-based milestone payments, (iii) up to $30.0 million of variable consideration in the form of sales-based milestone payments, and (iv) other royalty-based payments based on net sales. The event-based milestone payments are based on certain development and regulatory events occurring. We evaluated whether the milestone conditions have been achieved and if it is probable that a significant revenue reversal would not occur before recognizing the associated revenue. We determined that these milestone payments are not within our control or the licensee's control, such as regulatory approvals, and are not considered probable of being achieved until those approvals are received. Accordingly, we have fully constrained the $26.0 million of event-based milestone payments until such time that it is probable that significant revenue reversal would not occur. The sales-based milestone payments and other royalty-based payments are based on a level of sales for which the license is deemed to be the predominant item to which the royalties relate. We will recognize revenue for these payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. We received the $7.0 million of fixed consideration during the year ended December 31, 2020. To date, we have not recognized any sales-based or royalty revenue resulting from this licensing arrangement.

Under this arrangement, we recognized $7.0 million of revenue during the year ended December 31, 2020, which amount related solely to fixed consideration. We do not have any contract assets or contract liabilities as a result of this transaction.

Sublicense Agreement Relating to Rett Syndrome: In October 2020, we entered into a sublicense agreement with Taysha for a gene therapy for Rett syndrome and MECP2 gene constructs and regulation of their expression. The agreement grants Taysha worldwide exclusive rights to intellectual property developed by scientists at the University of North Carolina at Chapel Hill, the University of Edinburgh and us, and our know-how relating to the research, development, and manufacture of the gene therapy for Rett syndrome and MECP2 gene constructs and regulation of their expression.

We assessed the nature of the promised license to determine whether the license has significant stand-alone functionality and evaluated whether such functionality can be retained without ongoing activities by us and determined that the license has significant stand-alone functionality. Furthermore, we have no ongoing activities associated with the license to support or maintain the license's utility. Based on this, we determined that the pattern of transfer of control of the license to Taysha was at a point in time.

The transaction price of the contract includes (i) $3.0 million of fixed consideration, (ii) up to $26.5 million of variable consideration in the form of event-based milestone payments, (iii) up to $30.0 million of variable consideration in the form of sales-based milestone payments, and (iv) other royalty-based payments based on net sales. The event-based milestone payments are based on certain development and regulatory events occurring. We evaluated whether the milestone conditions have been achieved and if it is probable that a significant revenue reversal would not occur before recognizing the associated revenue. We determined that these milestone payments are not within our control or the licensee's control, such as regulatory approvals, and are not considered probable of being achieved until those approvals are received. Accordingly, we have fully constrained the $26.5 million of event-based milestone payments until such time that it is probable that significant revenue reversal would not occur. The sales-based milestone payments and other royalty-based payments are based on a level of sales for which the license is deemed to be the predominant item to which the royalties relate. We will recognize revenue for these payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. We received the $3.0 million of fixed consideration during the year ended December 31, 2020. To date, we have not recognized any sales-based or royalty revenue resulting from this licensing arrangement.

Under this arrangement, we recognized $3.0 million of revenue during the year ended December 31, 2020, which amount related solely to fixed consideration. We do not have any contract assets or contract liabilities as a result of this transaction.

NOTE 9 – STOCK-BASED COMPENSATION

We have two stock-based compensation plans as follows: (1) Abeona Therapeutics Inc. 2015 Equity Incentive Plan, which was approved by stockholders on May 7, 2015 and last amended on May 20, 2020 and (2) Abeona Therapeutics Inc. 2005 Equity Incentive Plan, which no further grants can be made under this plan.

Stock Option Repricing Program: On November 10, 2020, the Compensation Committee of the Company's Board of Directors (the "Compensation Committee") unanimously approved the repricing of all stock options outstanding under the Abeona Therapeutics Inc. 2015 Equity Incentive Plan held by current employees of the Company that had an exercise price per share between $1.16 and $17.30 (the "Eligible Stock Options"). As a result of the repricing, the exercise price of the Eligible Stock Options was set to $1.15 per share, equal to the closing sale price of the Company's common stock on November 10, 2020. Stock options held by members of the Board were not included in the repricing. Except for the modified exercise price, all other terms and conditions of each of the Eligible Stock Options remain in full force and effect. The fair value of the Eligible Stock Options was determined using the Hull White I lattice model. There were 79 grantees of Eligible Stock Options and the incremental compensation cost resulting from the modification was $0.6 million, of which $0.3 million was recognized as compensation expense during the year ended December 31, 2020. The expected weighted average period over which the remaining $0.3 million of incremental compensation costs will be recognized is 2.6 years.

On November 17, 2020, the Compensation Committee unanimously approved the repricing of all stock options outstanding under the Abeona Therapeutics Inc. 2015 Equity Incentive Plan and the Abeona Therapeutics Inc. 2005 Equity Incentive Plan held by the four current members of the Board that had an exercise price per share between $1.29 and $18.50 (the "Eligible Director Stock Options"). As a result of the repricing, the exercise price of the Eligible Director Stock Options was set to $1.28 per share, equal to the closing sale price of the Company's common stock on November 17, 2020. Except for the modified exercise price, all other terms and conditions of each of the Eligible Stock Options remain in full force and effect. The fair value of the Eligible Director Stock Options was determined using the Hull White I lattice model. There were four grantees of Eligible Director Stock Options and the incremental compensation cost resulting from the modification was $0.5 million, of which $0.4 million was recognized as compensation expense during the year ended December 31, 2020. The expected weighted average period over which the remaining $0.1 million of incremental compensation costs will be recognized is 2.4 years.

2015 Equity Incentive Plan

Under our 2015 Equity Incentive Plan, as amended, up to 18,000,000 shares of our authorized but unissued common stock are reserved for issuance to employees, consultants, or to non-employee members of the Board or to any member of the board of directors (or similar governing authority) of any affiliate of the Company. The maximum contractual term of awards is 10 years.

Stock Options: We estimate the fair value of each option award on the date of grant using the Black-Scholes option valuation model. We then recognize the grant date fair value of each option as compensation expense ratably using the straight-line attribution method over the service period (generally the vesting period). The Black-Scholes model incorporates the following assumptions:

- Expected volatility – we estimate the volatility of our share price at the date of grant using a "look-back" period which coincides with the expected term, defined below. We believe using a "look-back" period which coincides with the expected term is the most appropriate measure for determining expected volatility.
- Expected term – we estimate the expected term using the "simplified" method, as outlined in Staff Accounting Bulletin No. 107, "Share-Based Payment."
- Risk-free interest rate – we estimate the risk-free interest rate using the U.S. Treasury yield curve for periods equal to the expected term of the options in effect at the time of grant.
- Dividends – we use an expected dividend yield of zero because we have not declared or paid a cash dividend, nor do we have any plans to declare a dividend.

We used the following weighted-average assumptions to estimate the grant date fair value of the stock options granted for the years indicated:

	For the years ended December 31,	
	2020	**2019**
Expected volatility	110%	108%
Expected term	6.2 years	5.1 years
Risk-free interest rate	0.30%	2.21%
Expected dividend yield	0.00%	0.00%

We account for forfeitures as they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise.

Summarized stock option information for the 2015 Equity Incentive Plan is as follows:

	Options	Weighted-average exercise price
Outstanding options at January 1, 2019	5,525,405	$ 8.08
Granted, fair value of $5.14 per share	1,490,490	$ 6.53
Exercised	(303,129)	3.20
Expired/forfeited	(917,371)	7.95
Outstanding options at December 31, 2019	5,795,395	$ 7.96
Granted, fair value of $1.88 per share	2,645,146	$ 2.26
Exercised	(77,560)	2.28
Expired/forfeited	(2,802,242)	6.52
Outstanding options at December 31, 2020	5,560,739	$ 2.21
Non-vested options at December 31, 2019	2,342,706	$ 8.78
Non-vested options at December 31, 2020	2,507,203	$ 1.29

The weighted-average exercise price of stock options granted during the year ended December 31, 2020 was $1.42 after adjusting for the stock option repricing program noted above.

The intrinsic value related to the outstanding options under this plan was $1.7 million and $0.7 million, as of December 31, 2020 and 2019, respectively. The intrinsic value related to the exercisable options under this plan was $0.7 million and $0.6 million as of December 31, 2020 and 2019, respectively.

The total intrinsic value of the options exercised was $0 and $0.4 million during the years ended December 31, 2020 and 2019, respectively.

Further information regarding options outstanding under the 2015 Equity Incentive Plan as of December 31, 2020 is summarized below:

Range of exercise prices		Number of options outstanding	Weighted-average		Number of options exercisable	Weighted-average	
			Remaining life in years	Exercise price		Remaining life in years	Exercise price
$ 1.02	$ 1.28	4,562,630	7.8	$ 1.20	2,077,915	6.3	$ 1.23
2.31	2.59	161,642	1.4	2.31	161,642	1.4	2.31
4.38	4.78	357,925	3.2	4.43	357,925	3.2	4.43
6.59	7.42	298,865	2.6	7.33	298,865	2.6	7.33
8.54	13.65	66,567	6.5	13.26	47,817	6.3	13.10
14.45	16.02	113,110	1.1	15.96	109,372	1.0	15.96
		5,560,739			3,053,536		

As of December 31, 2020, the total compensation cost related to non-vested options not recognized is $7.8 million. The expected weighted average period over which the total compensation costs related to non-vested options will be recognized is 2.3 years.

Restricted Common Stock: Summarized stock option information for the 2015 Equity Incentive Plan is as follows:

	Restricted common stock awards	Weighted-average grant date fair value
Outstanding awards at January 1, 2019	-	$ -
Granted	376,625	$ 3.14
Vested	-	-
Forfeited	(22,000)	3.14
Outstanding awards at December 31, 2019	354,625	$ 3.14
Granted	5,290,312	$ 1.75
Vested	(817,054)	2.26
Forfeited	(1,875,384)	1.75
Outstanding awards at December 31, 2020	2,952,499	$ 1.78

The fair market value of the restricted common stock awards vested was $1.3 million and $0 during the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020, the total compensation cost related to restricted common stock not recognized is $4.1 million. The expected weighted average period over which the total compensation costs related to restricted common stock will be recognized is 1.8 years.

2005 Equity Incentive Plan

Under the 2005 Equity Incentive Plan, as amended, shares of our authorized but unissued common stock were reserved for issuance to employees, consultants, or to non-employee members of the Board or to any member of the board of directors (or similar governing authority) of any affiliate of the Company. As of January 20, 2015, no additional shares were available for grant under the 2005 Equity Incentive Plan. A total of 124,800 options were outstanding and exercisable under this plan as of December 31, 2020.

Summarized information for the 2005 Equity Incentive Plan is as follows:

	Options	Weighted-average exercise price
Outstanding options at January 1, 2019	316,400	$ 14.15
Expired/forfeited	(56,400)	19.75
Outstanding options at December 31, 2019	260,000	$ 12.94
Expired/forfeited	(135,200)	6.80
Outstanding options at December 31, 2020	124,800	$ 8.55

The intrinsic value related to the outstanding or exercisable options under this plan was $0 as of December 31, 2020 and 2019.

Further information regarding options outstanding under the 2005 Equity Incentive Plan as of December 31, 2020 is summarized below:

Range of exercise prices		Number of options outstanding	Weighted-average Remaining life in years	Weighted-average Exercise price	Number of options exercisable	Weighted-average Remaining life in years	Weighted-average Exercise price
$ 1.28	$ 1.28	80,000	3.2	$ 1.28	80,000	3.2	$ 1.28
11.50	18.50	42,000	2.4	18.17	42,000	2.4	18.17
30.50	113.50	2,800	0.6	72.00	2,800	0.6	72.00
		124,800			124,800		

NOTE 10 – 401(k) PLAN

We have a tax-qualified employee savings and retirement plan (the "401(k) Plan") covering all our employees in the United States. Pursuant to the 401(k) Plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit ($19,500 in 2020 and $19,000 in 2019) and to have the amount of such reduction contributed to the 401(k) Plan. The 401(k) Plan is intended to qualify under Section 401 of the Internal Revenue Code so that contributions by employees or by us to the 401(k) Plan, and income earned on 401(k) Plan contributions, are not taxable to employees until withdrawn from the 401(k) Plan, and so that contributions by us, if any, will be deductible by us when made. At the direction of each participant, we invest the assets of the 401(k) Plan in any of over 50 investment options. Company contributions under the 401(k) Plan were $0.3 million and $0.4 million for the years ended December 31, 2020 and 2019, respectively.

NOTE 11 - INCOME TAXES

Income tax expense differs from the statutory amounts for each of the following years:

	For the years ended December 31, 2020	2019
Income taxes at U.S. statutory rate	$ (17,689,000)	$ (16,020,000)
Current year reserve	12,020,000	15,976,000
Expenses not deductible	5,669,000	44,000
Total tax expense	$ -	$ -

Deferred taxes are provided for the temporary differences between the financial reporting bases and the tax bases of our assets and liabilities. The temporary differences that give rise to deferred tax assets and liabilities were as follows:

	December 31, 2020	December 31, 2019
Deferred tax assets (liabilities):		
Net operating loss carryforwards	$ 61,062,000	$ 50,802,000
General business credit carryforwards	4,398,000	3,939,000
State credits	2,857,000	2,934,000
Property, equipment and goodwill	8,000	(28,000)
Stock options	9,551,000	7,960,000
Deferred revenue	62,000	62,000
Intangible assets	312,000	1,625,000
Other	70,000	28,000
Gross deferred tax assets	78,320,000	67,322,000
Valuation allowance	(78,320,000)	(67,322,000)
Net deferred taxes	$ -	$ -

As of December 31, 2020, we had approximately $290.8 million of net operating loss carryforwards and approximately $4.4 million of general business credit carryforwards. These carryforwards expire as follows:

	Net operating loss carryforwards	General business credit carryforwards
2021	$ 5,378,000	$ 56,000
2022	8,230,000	431,000
2023	5,434,000	362,000
2024	8,711,000	287,000
2025	2,370,000	182,000
Thereafter	97,576,000	3,080,000
	$ 127,699,000	$ 4,398,000

As of December 31, 2020, we had approximately $163.1 million of net operating loss carryforwards that do not expire and can be carried forward indefinitely.

We acquired MacroChem Corporation on February 25, 2009 and Somanta Pharmaceuticals, Inc. on January 4, 2008. Both of these corporations were loss-making entities at the time of acquisition. As a result, the net operating losses related to those acquisitions may be subject to annual limitations as well.

NOTE 12 – COMMITMENTS AND CONTINGENCIES

Arbitration Proceeding

We are currently engaged in an arbitration proceeding with REGENXBIO regarding the former license agreement between the parties relating to use of the AAV9 capsid in our MPS IIIA, MPS IIIB, CLN1 (which has now been sold to Taysha Gene Therapies, as discussed in Note 8 above), and CLN3 programs. The license terminated on May 2, 2020, and on May 25, 2020, we filed an arbitration claim with the American Arbitration Association ("AAA") alleging that REGENXBIO materially breached the license agreement prior to termination and seeking, among other things, a declaration that as a result of REGENXBIO's material breach, we are not responsible for payments totaling $28 million (which would otherwise have been due in 2020) plus accrued interest ($3.5 million as of December 31, 2020). REGENXBIO disputes our arbitration claim and has filed a counterclaim seeking payment of these amounts. An arbitration hearing before a tribunal of three AAA arbitrators was held on March 8 and March 9, 2021. The tribunal has not yet issued its opinion, and based on the post-hearing schedule an opinion is expected in late second quarter 2021 or early third quarter 2021.

Operating Leases

We lease space under operating leases for manufacturing and laboratory facilities and administrative offices in Cleveland, Ohio, as well as administrative offices in New York, New York. We also lease office space in Madrid, Spain as well as certain office equipment under operating leases, which have a non-cancelable lease term of less than one year and, therefore, we have elected the practical expedient to exclude these short-term leases from our right-of-use assets and lease liabilities.

Components of lease cost under ASC 842 for the years ended December 31, 2020 and 2019 are as follows:

	For the years ended December 31,	
	2020	2019
Operating lease cost	$ 1,736,000	$ 1,591,000
Variable lease cost	$ 337,000	$ 322,000
Short-term lease cost	$ 61,000	$ 133,000

The following table presents information about the amount and timing of cash flows arising from operating leases under ASC 842 as of December 31, 2020:

Maturity of lease liabilities:		
2021	$	1,713,000
2022		1,727,000
2023		1,741,000
2024		1,781,000
2025		1,799,000
Thereafter		87,000
Total undiscounted operating lease payments		8,848,000
Less: imputed interest		1,875,000
Present value of operating lease liabilities	$	6,973,000
Balance sheet classification:		
Current portion of lease liability	$	1,713,000
Long-term lease liability		5,260,000
Total operating lease liabilities	$	6,973,000
Other information:		
Weighted-average remaining lease term for operating leases		61 months
Weighted-average discount rate for operating leases		9.6%

EXHIBIT 21

Subsidiaries of the Registrant

Abeona Therapeutics LLC, an Ohio company

Abeona Therapeutics Europe, S.L., a Spanish company

MacroChem Corporation, a Delaware company

Virium Pharmaceuticals, Inc., a Delaware company

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements No. 333-197220 on Form S-1, Nos. 333-204179, 333-205128 and 333-224867 on Form S-3, and Nos. 333-125796, 333-161642, 333-169067, 333-189985, 333-204055, 333-214846, 333-221552 and 333-238571 on Form S-8 Abeona Therapeutics Inc. and Subsidiaries, of our report dated March 24, 2021, relating to the consolidated financial statements appearing in this Annual Report on Form 10-K of Abeona Therapeutics Inc. and Subsidiaries for the year ended December 31, 2020.

/s/ WHITLEY PENN LLP

Plano, Texas
March 24, 2021

EXHIBIT 31.1

PRINCIPAL EXECUTIVE OFFICER CERTIFICATION PURSUANT TO 18 U.S.C.
SECTION 1350, AS ADOPTED PURSUANT TO SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002

I, Michael Amoroso, certify that:

1. I have reviewed this Annual Report on Form 10-K of Abeona Therapeutics Inc.;

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

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

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

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

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

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

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

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

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

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

Dated: March 24, 2021

/s/ Michael Amoroso

Michael Amoroso
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

PRINCIPAL FINANCIAL OFFICER CERTIFICATION PURSUANT TO 18 U.S.C.
SECTION 1350, AS ADOPTED PURSUANT TO SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002

I, Edward Carr, certify that:

1. I have reviewed this Annual Report on Form 10-K of Abeona Therapeutics Inc.;

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

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

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

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

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

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

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

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

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

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

Dated: March 24, 2021

/s/ Edward Carr
Edward Carr
Chief Accounting Officer
(Principal Financial Officer)

EXHIBIT 32

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

In connection with the Annual Report of Abeona Therapeutics Inc. (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, Michael Amoroso, President and Chief Executive Officer of the Company, and Edward Carr, Chief Accounting Officer of the Company, each certify, pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 24, 2021

By: */s/ Michael Amoroso*
Michael Amoroso
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 24, 2021

By: */s/ Edward Carr*
Edward Carr
Chief Accounting Officer
(Principal Financial Officer)