UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 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 001-36510

LARIMAR THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-3857670**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
Three Bala Plaza East, Suite 506 Bala Cynwyd, Pennsylvania	**19004**
(Address of principal executive offices)	(Zip Code)

(844) 511-9056

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	LRMR	The Nasdaq Global Market

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 the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant 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. ☐

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

On the last business day of the most recently completed second fiscal quarter, the aggregate market value (based on the closing sale price of its common stock on that date) of the voting and non-voting stock held by non-affiliates of the registrant was $123.3 million.

As of March 2, 2021, the registrant had 15,367,730 shares of the registrant's Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates certain information by reference from the registrant's proxy statement for the 2021 annual meeting of shareholders to be filed no later than 120 days after the end of the registrant's fiscal year ended December 31, 2020.

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As previously disclosed, on May 28, 2020, Zafgen, Inc., a Delaware corporation ("Zafgen"), completed a Merger with Chondrial Therapeutics, Inc., a Delaware corporation ("Chondrial"), in accordance with the terms of the Agreement and Plan of Merger Reorganization (the "Merger Agreement") entered into on December 17, 2019. Pursuant to the Merger Agreement, (i) a subsidiary of Zafgen merged with and into Chondrial, with Chondrial continuing as a wholly-owned subsidiary of Zafgen and the surviving corporation of the merger and (ii) Zafgen was renamed as "Larimar Therapeutics, Inc." (the "Merger").

For accounting purposes, the Merger is treated as a "reverse asset acquisition" under generally accepted accounting principles in the United States ("GAAP") and Chondrial is considered the acquirer. Accordingly, Chondrial's historical results of operations will replace the Company's (as defined below) historical results of operations for all periods prior to the Merger and, for all periods following the Merger, the results of operations of the combined company will be included in the Company's financial statements.

This annual report on Form 10-K relates to the Company's fiscal year ended December 31, 2020 and is therefore the Company's first annual report that includes results of operations for the combined company, including Chondrial.

Unless the context otherwise requires, references to the "Company," the "combined company," "we," "our" or "us" in this report refer to Larimar Therapeutics, Inc. and its subsidiaries, references to "Larimar" refer to the Company following the completion of the Merger and references to "Zafgen" refer to the Company prior to the completion of the Merger.

Except as otherwise noted, references to "common stock" in this report refer to common stock, $0.001 par value per share, of the Company.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements made in this Annual Report on Form 10-K that are not statements of historical or current facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements discuss our business, operations and financial performance and conditions, as well as our plans, objectives and expectations for our business operations and financial performance and condition. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "positioned," "potential," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. In addition, statements that "we believe" or similar statements reflect our beliefs and opinions on the relevant subject. These forward-looking statements, which are subject to risks, uncertainties and assumptions about us, may include projections of our future financial performance, our anticipated growth strategies and anticipated trends in our business.

You should understand that the following important factors could affect our future results and could cause those results or other outcomes to differ materially from those expressed or implied in our forward-looking statements:

- our estimates regarding future results of operations, financial position, research and development costs, capital requirements and our needs for additional financing;
- how long we can continue to fund our operations with our existing cash, cash equivalents and marketable debt securities;
- our ability to optimize and scale CTI-1601 or any other product candidate's manufacturing process and to manufacture sufficient quantities of clinical and, if approved, commercial supplies of CTI-1601;
- our ability to realize any value from CTI-1601 and any other product candidate we may develop in the future in light of inherent risks and difficulties involved in successfully bringing product candidates to market and the risk that products will not achieve broad market acceptance;
- delays or changes in our anticipated clinical timelines, including as a result of patient recruitment, changes in clinical protocols and milestones for CTI-1601, including those associated with COVID-19;
- uncertainties in obtaining successful clinical results (including demonstrating safety, tolerability and efficacy profiles that are satisfactory to the FDA, EMA and other comparable regulatory authorities for marketing approval) for CTI-1601 or any other product candidate that we may develop in the future and unexpected costs that may result therefrom;
- our ability to comply with regulatory requirements applicable to our business and other regulatory developments in the United States and foreign countries;
- the uncertainties associated with the clinical development and regulatory approval for CTI-1601 or any other product candidate that we may develop in the future, including potential delays in the commencement, enrollment and completion of clinical trials;
- the difficulties and expenses associated with obtaining and maintaining regulatory approval for CTI-1601 or any other product candidate we may develop in the future, and the indication and labeling under any such approval;
- the size and growth of the potential markets for CTI-1601 or any other product candidate that we may develop in the future, the rate and degree of market acceptance of CTI-1601 or any other product candidate that we may develop in the future and our ability to serve those markets;

- the success of competing therapies and products that are or become available;
- our ability to obtain and maintain patent protection and defend our intellectual property rights against third-parties;
- the performance of third-parties upon which we depend, including third-party contract research organizations, or CROs, and third-party suppliers, manufacturers, group purchasing organizations, distributors, and logistics providers;
- our ability to maintain our relationships and contracts with our key vendors;
- our ability to recruit or retain key scientific, technical, commercial, and management personnel or to retain our executive officers;
- our ability to maintain proper functionality and security of our internal computer and information systems and prevent or avoid cyber-attacks, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption; and
- the extent to which health epidemics and other outbreaks of communicable diseases, including the ongoing COVID-19 pandemic, disrupt our operations, the operations of third parties on which we rely or the operations of regulatory agencies we interact with in the development of CTI-1601.

These forward-looking statements are based on management's current expectations, estimates, forecasts and projections about our business and the industry in which we operate, and management's beliefs and assumptions are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe the expectations reflected in the forward-looking statements are reasonable, the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements may not be achieved or occur at all. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this Annual Report on Form 10-K or to reflect the occurrence of any unanticipated events. Comparisons of results for current and any prior periods are not intended to express any future trends on indications of future performance, unless expressed as such, and should only be viewed as historical data.

SUMMARY RISK FACTORS

The risk factors summarized and detailed below could materially harm our business, operating results and/or financial condition, impair our future prospects and/or cause the price of our common stock to decline. These are not all of the risks we face, and other factors not presently known to us or that we currently believe are immaterial may also affect our business if they occur. Material risks that may affect our business, operating results and financial condition include, but are not necessarily limited to, those relating to:

Risks Related to Our Financial Position and Need for Capital

- We have incurred significant losses since our inception and anticipate that we will incur continued losses for the foreseeable future.
- We have no commercial revenue and may never become profitable.
- We need to raise additional funding. This funding may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed would force us to delay, limit or terminate our product development efforts or other operations.

Risks Related to Our Product Development and Regulatory Approvals

- Our success is currently dependent upon the success of our sole product candidate, CTI-1601, which is currently in Phase 1 clinical trials. We cannot be certain that we will be successful with our clinical development or that we will be able to obtain regulatory approval for CTI-1601.
- Clinical development is a lengthy and expensive process with an uncertain outcome, and the results of nonclinical studies, toxicology studies or clinical trials may not be predictive of future nonclinical studies, toxicology studies or clinical trial results.
- Failure or delays in optimizing and scaling CTI-1601 or any other product candidate's manufacturing process may not allow us to manufacture sufficient quantities of clinical and, if approved, commercial supplies of CTI-1601.
- Failures or delays in the completion of our clinical trials could result in increased costs and could delay, prevent or limit our ability to generate revenue and continue our business.
- CTI-1601 may cause adverse events or undesirable side effects that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if any.
- Changes in regulatory requirements, FDA guidance, guidance from other regulatory authorities or unanticipated events during our clinical trials of CTI-1601 may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline.
- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell CTI-1601, we may not be able to generate any revenue.
- Even if we receive regulatory approval for CTI-1601, we may not achieve broad market acceptance, which would limit the revenue that we generate from our sales.
- Even if we obtain regulatory approval for CTI-1601, it will remain subject to extensive regulatory oversight.

Risks Related to Our Business

- If we are unable to manage expected growth in the scale and complexity of our operations, including attracting and hiring additional qualified management, our performance may suffer.
- We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions or alliances.
- We are subject to healthcare laws and regulations, and health information privacy and security laws, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Risks Related to Our Reliance on Third Parties

- We have limited experience in conducting or supervising clinical trials and must outsource all clinical trials. As a result, many important aspects of our drug development programs are outside of our direct control.
- We rely on third-party supply and manufacturing partners for drug supplies for our research and development, nonclinical activities, and clinical activities, and may do the same for any commercial

supplies of our product candidates.

Risks Related to Our Intellectual Property Rights

- If we are unable to adequately protect our proprietary technology or maintain issued patents which are sufficient to protect CTI-1601 or potential product candidates, third parties could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
- Certain of the patents we license relating to CTI-1601 will expire by 2025 and we will lose our ability to rely upon these patents to prevent competing products, and certain patent applications we license relating to CTI-1601 which would be expected to expire in 2040 may not issue as patents, and the claims of any patents that issue may not provide sufficient protection from competitors or other third parties, which may impair our ability to generate revenue.
- Certain provisional and non-provisional patent applications that we own relating to our platform technology may not issue as patents, and the claims of any patents that issue may not provide sufficient protection from competitors or other third parties for potential product candidates, which may impair our ability to generate revenue.
- We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing CTI-1601 or other potential product candidates, if approved.
- We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.
- Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.
- We are dependent on licensed intellectual property for CTI-1601. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing CTI-1601, if approved.

Risks Related to Our Common Stock

- Our stock price could be highly volatile, with limited trading liquidity and purchasers of our common stock could incur substantial losses.
- We must maintain effective internal controls over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.
- Ownership of our common stock is highly concentrated, and it may prevent other stockholders from influencing significant corporate decisions.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage biotechnology company focused on developing treatments for patients suffering from complex rare diseases using our novel cell penetrating peptide technology platform. Our lead product candidate, CTI-1601, is a subcutaneously administered, recombinant fusion protein intended to deliver human frataxin, or FXN, an essential protein, to the mitochondria of patients with Friedreich's ataxia. Friedreich's ataxia is a rare, progressive and fatal disease in which patients are unable to produce sufficient FXN due to a genetic abnormality. There is currently no effective therapy for Friedreich's ataxia. CTI-1601 is currently being evaluated in Phase 1 clinical trials in patients with Friedreich's ataxia. We have received orphan drug status, fast track designation and rare pediatric disease designation, from the U.S. Food and Drug Administration, or the FDA, for CTI-1601. In addition, we received orphan drug designation for CTI-1601 from the European Commission. The receipt of such designations or positive opinions may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA or European Medicines Agency, or EMA, procedures and does not assure ultimate approval by the FDA or EMA.

We believe that our cell penetrating peptide, or CPP, technology platform, which enables a therapeutic molecule to cross a cell membrane in order to reach intracellular targets, has the potential to enable the treatment of other rare and orphan diseases. We intend to use our proprietary platform to target additional orphan indications characterized by deficiencies in or alterations of intracellular content or activity.

We have assembled an experienced management team, each of whom has over 20 years of pharmaceutical industry experience. Our management team and consultants have significant expertise in discovery, nonclinical and clinical development, regulatory affairs and the development of manufacturing processes utilizing good manufacturing practices, or GMPs, for biologics and small molecules. We believe that our management team's diverse mix of skills provides for the implementation of effective approaches to drug and biologic development.

Our Strategy

Our strategy is to become a leader in the treatment of rare diseases by leveraging our technology platform and applying our management team's know how and expertise to the development of CTI-1601 and other future pipeline programs. Key elements of our strategy include:

- Advance CTI-1601 through Clinical Development and Regulatory Approval in the United States the European Union, or EU, and other foreign jurisdictions. CTI-1601 is currently in Phase 1 clinical trials in the United States. We are collaborating with key opinion leaders and seeking guidance from regulatory authorities to develop a clinical development plan for regulatory approval of CTI-1601 in the United States, the EU, the UK, Australia and Canada...

- ***If CTI-1601 receives regulatory approvals, commercialize CTI-1601 in the United States, the EU, and other relevant countries independently or with third parties***. We intend to evaluate commercialization options in the United States the EU and in other foreign jurisdictions throughout the world where Friedreich's ataxia patients can benefit. We may build our own internal sales force; we may enter into a joint marketing partnership with another pharmaceutical or biotechnology company, whereby it may jointly sell and market CTI-1601; or we may seek to out-license CTI-1601, whereby other pharmaceutical or biotechnology companies sell and market CTI-1601 and pay us milestone and/or royalty payments on sales.

- ***Expand Our Product Candidate Pipeline to Treat a Variety of Rare Diseases***. We intend to expand our pipeline to treat additional rare diseases. A key component of this strategy is to utilize our novel protein replacement therapy platform technology to deliver FXN or other molecules to intracellular targets. We employ a rational approach to selecting disease targets, and take into account many scientific, business, and indication specific factors before choosing each indication.

- ***Continue to Improve Our Novel Protein Replacement Therapy Platform***. We continue to improve the scientific understanding of our platform, including how our technology allows enhanced delivery of cargo proteins, thereby impacting the biological processes associated with the diseases we seek to treat. In addition, with our expertise in the use of a CPP, to effectively deliver proteins to intracellular targets, we believe that our scientists are well positioned to design and develop additional therapies that will address unmet medical needs associated with other rare diseases. We also plan to continue to build our intellectual property estate to improve our protein replacement therapy platform.

- ***Continue to Strengthen Key Relationships***. We partner with experts in every aspect of development. We believe this expertise, along with our technology platform, will provide us with the ability to develop and commercialize the drug and biologic candidates we have under development and to maximize the value of our platform. In addition to partnering with experts in drug and biologic development, we collaborate with key opinion leaders, academic institutions, experts in the field of rare diseases and with patient advocacy groups associated with the diseases that are being targeted. We have established a scientific advisory board and we regularly seek advice and input from these experienced thought leaders on matters related to our research and development programs. The members of our scientific advisory board consist of distinguished research scientists, professors and industry experts recognized as key opinion leaders in the fields of rare disease, pediatrics and mitochondrial disease. We build these relationships to enhance our knowledge of the patient's needs and utilize that knowledge to design development programs intended to address unmet medical needs and add value for the patient.

Platform Technology for Treatment of Rare Genetic Diseases

There are estimated to be between 5,000 and 7,000 rare genetic diseases, which, collectively affect hundreds of millions of people worldwide. Of the hundreds of millions of individuals suffering from these rare genetic diseases, only 5% have therapeutic options available to manage their disease. Many of these diseases result from a deficiency in the amount or the function of a particular target molecule, often a protein. Particularly challenging to treat are those diseases that result from the deficiency of a molecule that is active within a cell or within a cell-based organelle. The challenge to providing treatment of these diseases is the need to improve the amount or function of the therapeutic target by transporting a therapeutic element across the cell membrane and potentially the membrane of the organelle where the target is active in the diseased patients.

The ability to transport therapeutic proteins across biological membranes has, to date, not been reproducibly achieved. The collective population of people with rare diseases stands to benefit from the emergence of a scalable treatment platform that can transport therapeutics across cell membranes to deliver them to the intracellular site of activity. In addition, traditionally, medical treatment for each rare genetic disorder has been approached on a disease-by-disease basis. This approach is inefficient, as there are thousands of diseases, each with a distinct patient population, that cannot be addressed by traditional therapeutic approaches and are in need of treatment options. Our understanding of our therapeutics derived from proprietary gene expression data across several disease models supports the concept that product candidates based on our platform technology could significantly impact common pathological mechanisms in various diseases with comparable etiologies. We are utilizing this approach to identify therapeutic opportunities where our molecules and technology are more likely to be impactful.

Lead Product Candidate—CTI-1601 For the Treatment of Friedreich's ataxia

Friedreich's ataxia

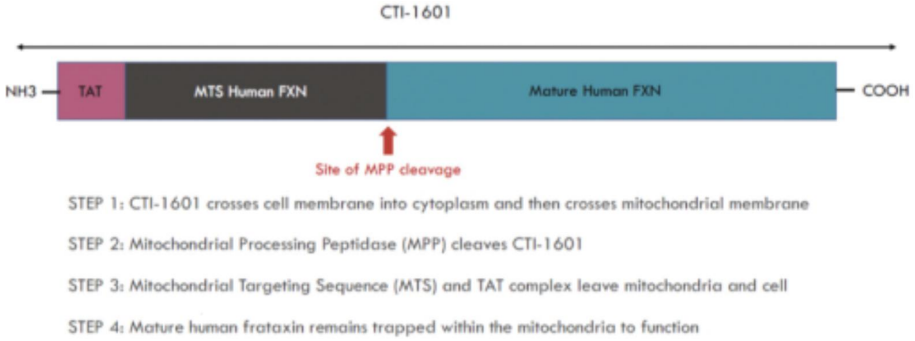
Friedreich's ataxia is a rare genetic disease that is the most common inherited ataxia in humans, with an estimated 4,000-5,000 individuals living with Friedreich's ataxia in the United States and between 18,000 and 20,000 patients affected by the condition in the EU and the United Kingdom. Friedreich's ataxia results from a deficiency of the mitochondrial protein, FXN. FXN is an essential and phylogenetically conserved protein that is found in cells throughout the body, with highest levels found in the heart, spinal cord, liver, pancreas, and skeletal muscle. FXN is encoded in the nucleus, expressed in the cytoplasm and transported into the mitochondria, where it is processed to the mature form. As part of this process the mitochondrial targeting sequence is cleaved off in the mitochondria by a naturally occurring enzyme.

Friedreich's ataxia is a progressive multi-symptom disease typically presenting in mid-childhood that affects the functioning of multiple organs and systems. It is a debilitating neurodegenerative disease that results in poor coordination of legs and arms, progressive loss of the ability to walk, generalized weakness, loss of sensation, scoliosis, diabetes and cardiomyopathy as well as impaired vision, hearing and speech. Patients suffer from progressive neurologic and cardiac dysfunction. Key among these is a primary neurodegeneration of the dorsal root ganglia and the dentate nucleus of the cerebellum, which leads to the hallmark clinical findings of progressive limb ataxia and dysarthria. A hypertrophic cardiomyopathy is common and associated with early mortality, typically between 30 and 50 years of age. As of March 2021, there are no medical treatment options approved for the treatment of Friedreich's ataxia.

CTI-1601

CTI-1601, a biologic fusion protein that is administered subcutaneously, consists of a CPP genetically fused to human FXN, and includes a mitochondrial targeting sequence. Using our proprietary peptide delivery technology, CTI-1601 carries the molecule from the intravascular space across the cell membrane and into the mitochondria where the CPP and the mitochondrial targeting sequence are cleaved off to yield mature FXN. See Figure 1.

Figure 1.



CTI-1601 is currently being evaluated in Phase 1 clinical trials. Based solely on the results of our nonclinical development program, we believe that administering CTI-1601 may increase FXN levels in the mitochondria of patients with Friedreich's ataxia and patients could potentially experience:

- improved cellular function;
- a positive impact on Friedreich's ataxia symptoms; and
- a slowing of progression of the disease, potentially prolonging life.

Our knowledge of CTI-1601 and of the impact of CTI-1601 on gene expression gives our scientists the ability to identify potential additional disease indications based on similar alterations of genomic, lipidomic and proteomic patterns in rare diseases models. Thus, our technology may allow us to address other rare genetic diseases that either require the replacement of molecules that need to target specific intracellular organelles, or that share alteration patterns that overlap and that are impacted by treatment with CTI-1601. Finally, the use of CTI-1601 to improve mitochondrial function in other rare diseases that demonstrate evidence of mitochondrial dysfunction is also being explored.

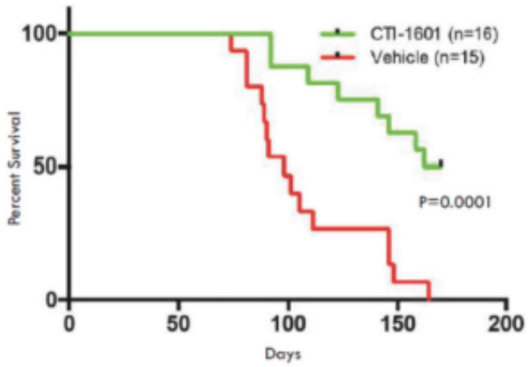
Development of CTI-1601

Nonclinical Development

Knock-Out Mice Studies

CTI-1601 has been demonstrated to prolong the life of knock-out mice or KO mice whose heart and skeletal muscles were deficient in FXN. These mice, when untreated, develop a severe hypertrophic cardiomyopathy similar to patients with Friedreich's ataxia and, like many Friedreich's ataxia patients, die early in life. In nonclinical studies of CTI-1601, the median survival in animals treated with vehicle of 98 days was extended to a median survival of 166 days in animals treated with CTI-1601 subcutaneously three times per week (p=0.0001). Furthermore, 87.5% of mice treated with CTI-1601 survived beyond the mean age of death in the vehicle treated group (107.5 days) whereas only 33% of vehicle treated animals survived. Results are reflected in Figure 2.

Figure 2.



In a second study conducted at an independent laboratory, a similar mouse model was studied. In this study doses of 2 mg/kg, 10 mg/kg, 30 mg/kg, 60 mg/kg and 100 mg/kg administered subcutaneously every other day were compared to vehicle. After 2 weeks of dosing, mitochondrial extracts from cardiac tissue were analyzed for the presence of human FXN. In addition, activity of succinate dehydrogenase, or SDH, an enzyme whose activity is dependent on the presence of FXN, was also analyzed. Human FXN was found in the mitochondria of the cardiomyocytes and increased with increasing dose. SDH activity which was suppressed to near zero in vehicle treated animals was also suppressed to near zero in the 2 mg/kg dose group. In the 10 mg/kg dose group activity was increased and in the 30 mg/kg dose group the activity was returned to that of wild type animals. There was no further increase in activity when the animals were dosed with 60 mg/kg or 100 mg/kg but the effect was maintained at levels equivalent to that of wild type animals. See Figure 3 and 4.

Figure 3.

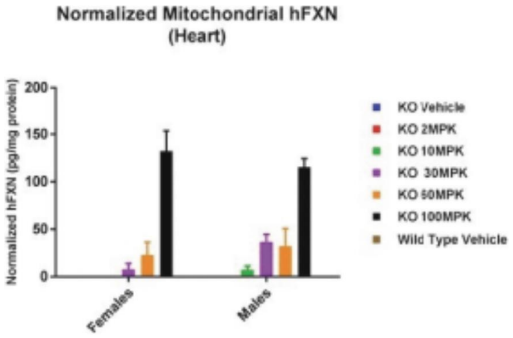
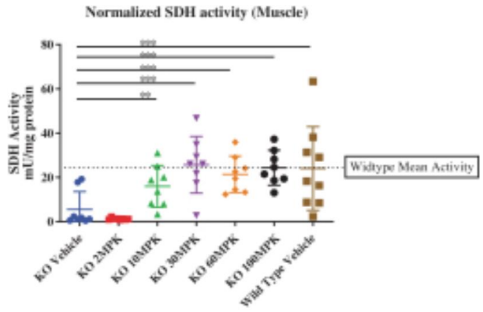


Figure 4.



A third study, also performed at an independent laboratory, demonstrated the maintenance of cardiac function when the same KO mouse model was studied. These mice were treated with CTI-1601 at doses of 10 mg/kg every other day for 6 weeks. Echocardiograms were performed prior to initiating dosing and after 4 weeks of dosing. When compared to vehicle, mice treated with CTI-1601 maintained their left ventricular volume and ejection fraction while vehicle treated mice deteriorated over the same 4-week period. See Figures 5 and 6.

Figure 5.

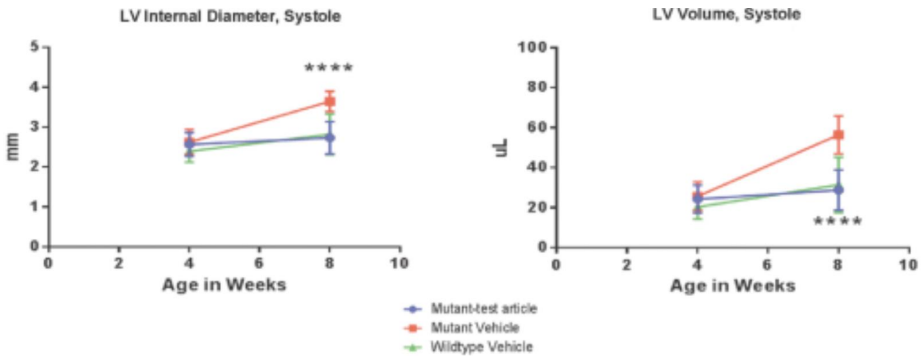
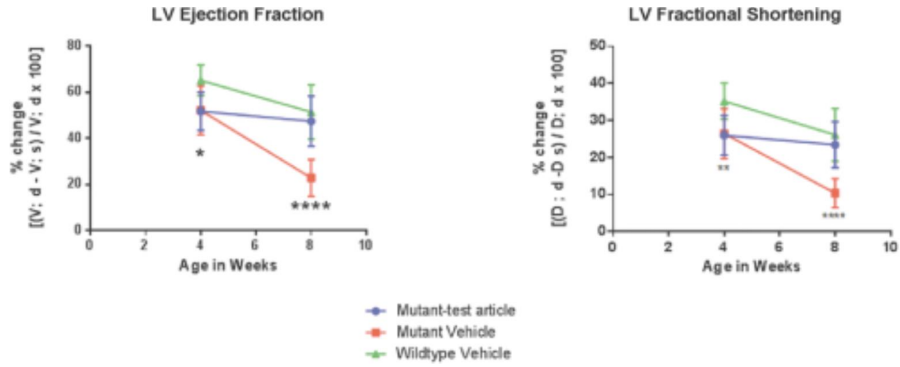


Figure 6.



Using a neurologic mouse model, treatment with CTI-1601 prevented the development of ataxia in mice whose nervous system was deficient in FXN compared to those treated with placebo.

In multiple nonclinical studies in rodents and non-human primates, or **NHPs**, human FXN was found to be distributed into all tissues tested following CTI-1601 dosing. See Figure 7.

Figure 7.

Observed hFXN across all tissue and cell types tested:

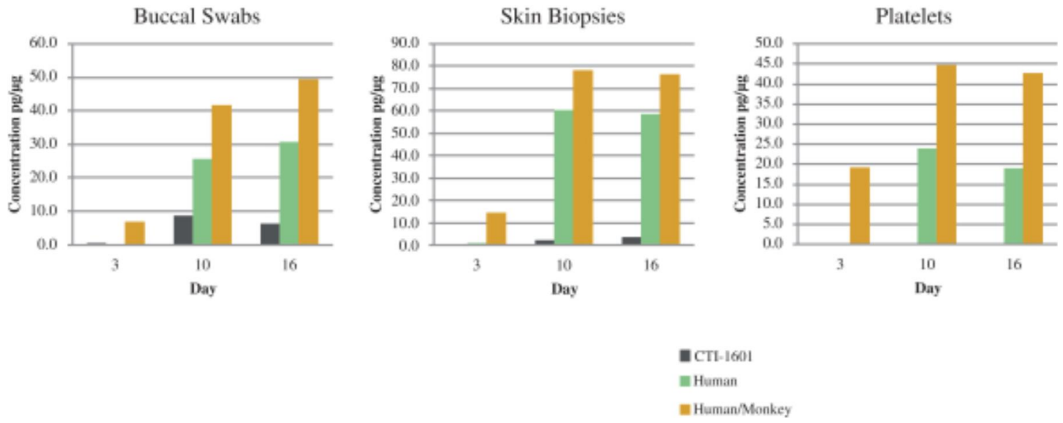
✓ Brain	✓ Spinal Cord	✓ Skin
✓ Heart	✓ Cardiac Mitochondria	✓ Buccal Cells
✓ Liver	✓ CSF (Cerebrospinal Fluid)	✓ Platelets
✓ Dorsal Root Ganglia	✓ Skeletal Muscle	

Tissues Examined, By Study

Study	Study Vehicle	Human Frataxin Distribution
TOX-1601-01	Rats	Brain, Heart, Liver
PHARM-1601-02	Neuro KO Mice	Brain, Dorsal Root Ganglia, Spinal Cord
PHARM-1601-03	Cardiac KO Mice	Mitochondria of Skeletal Muscle and Cardiomyocytes
PK-1601-08	Cynomolgus Monkey	CSF, Skin, Buccal Cells, Platelets

Since CTI-1601 is intended to increase FXN levels in patients with Friedreich's ataxia who are deficient in FXN, it is important to be able to measure changes in human FXN in the clinic in easily accessible tissues. To accomplish this, we have developed an assay that can measure and quantify human FXN in buccal swabs skin biopsies and platelets. This process is designed to allow repeated analysis of changes in human FXN in patients over time as they are dosed with CTI-1601. The effectiveness of this assay was demonstrated in NHPs dosed for 14 days with 15 mg/kg twice a day of CTI-1601. Buccal swabs skin biopsies and platelets were obtained on Day 3 prior to administration of any CTI-1601 but after two days of dosing with vehicle. No human FXN was found. Since these were healthy NHPs there were levels of endogenous monkey FXN present. This is demonstrated by the yellow bars in the graph in Figure 8 below on Day 3. After 7 and 14 days of dosing with CTI-1601 human FXN was seen in significant amounts in all tissues analyzed. This is demonstrated by the appearance of the green bars on Day 10 and 16 in the figure below. This study demonstrates that CTI-1601 delivers human FXN to NHPs when administered subcutaneously and that we should be able to use our proprietary assay to evaluate change in FXN level in patients with Friedreich's ataxia as CTI-1601 enters early-stage clinical trials.

Figure 8.



Non-Human Primate and Rat Studies

We have conducted 28-day and 13-week GLP toxicology studies for CTI-1601 in two species, rat and NHP. In the rat studies, some injection sites showed edema and erythema with associated histologic changes localized to the injection site. The rat studies showed no significant clinical observations and no significant systemic histopathological findings. In the NHP studies, some injection sites were raised and firm with dose dependent histologic changes around the injection sites. The NHP 28-day study showed no systemic toxicity. The NHP 13-week study showed no systemic toxicity in the low dose group, and minimal to mild histopathological findings in the high dose group. There were also several episodes of occasional transient rigidity in some animals observed immediately after dosing in the two highest dose groups at very high exposures. These clinical observations resolved with no intervention and all of the NHPs who experienced these clinical observations received all doses and completed the in-life portion of the study. We are progressing our toxicology program to support chronic dosing of CTI-1601 and are performing all required studies to support a BLA submission. The results from these toxicology studies cannot be predicted and could affect the timing and design of the development program for CTI-1601 as well as have an impact on the future safety profile of CTI-1601.

Clinical Development

We continue to plan and perform toxicology studies required by FDA to support future clinical studies. We intend to continue to work closely with the FDA regarding design and timing of the other required studies.

Clinical Trials

We submitted our IND application for CTI-1601 in September of 2019 and began Phase 1 clinical trials in December of 2019 in patients with Friedreich's ataxia. The design of the clinical trials included a Phase 1 Single Ascending Dose, or SAD trial. The primary objective of the SAD study was to assess the safety and tolerability of increasing doses of CTI-1601 when administered subcutaneously to patients with Friedreich's ataxia who are 18 years of age and older. Patients received either CTI-1601 or placebo. Pharmacokinetics and pharmacodynamics were also being assessed. The first two cohorts of this study were dosed prior to March of 2020 after which we paused the study due to concerns about patient safety given the COVID-19 pandemic. After implementing additional patient safety procedures, we dosed the third cohort of this study in July 2020. In December 2020 we announced the completion of dosing of the Phase 1 SAD trial. A safety review committee reviewed preliminary blinded data after each cohort of the SAD trial. Based on preliminary data, single subcutaneous injections of CTI-1601 at doses up to 100 mg are thought to have been well tolerated. During the trials, mild and transient injection site adverse events were reported and no serious adverse events were reported. At all doses tested, the Phase 1 SAD data support further investigation of CTI-1601Our analysis of the clinical trial results remains ongoing.

In August 2020 we initiated a multiple ascending dose or MAD trial in patients with Friedreich's ataxia which is currently planned to have three cohorts. The third cohort in this study was dosed in the first quarter of 2021. Based on data from the initial three cohorts we will assess whether to close out the MAD trial as planned or whether to add a fourth cohort to enhance our understanding of the safety and tolerability, PK and PD of CTI-1601. As in the SAD study the primary endpoint for the MAD study is safety and tolerability. Also, as in the SAD clinical trial, pharmacokinetics will be assessed. In addition, we will be measuring changes in FXN level over the course of treatment to determine if an increase in FXN in peripheral tissues is achieved.

Development Plan

We expect to initiate an open label extension, or OLE, which we refer to as the JIVE study, in the second half of 2021. The JIVE study is a clinical trial that will enroll patients who participated in the SAD or MAD study if they are eligible and is designed to gather long-term safety and tolerability data. In the SAD and MAD clinical studies patients received either CTI-1601 or placebo while in our JIVE study, all patients will receive CTI-1601.

We expect to initiate a MAD placebo-controlled study of CTI-1601 in patients under 18 years of age in the second half of 2021. These patients may also be eligible to enroll in the JIVE study after completing participation in the MAD study.

We expect to initiate a registration study once enough data to inform on dosing and trial design has been obtained. This is currently planned for the second half of 2022. This study's design and protocol will be based on the results of the earlier studies and will incorporate feedback we receive from discussions with the regulatory authorities.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop into products and commercialize may compete with existing therapies and new therapies that may become available in the future. While we believe that our platform technology, product candidates and scientific expertise in the field of rare diseases provide competitive advantages, we face competition from various sources, including larger and better-funded pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

CTI-1601 may compete with other therapies in development for Friedreich's ataxia, including development programs by Reata Pharmaceuticals, Inc., PTC Therapeutics, Retrotope, Minoryx Therapeutics, Frategene and. Exicure as well as companies applying gene therapy technologies such as Neurocrine, Novartis, Takeda, Pfizer, Sarepta (Aavanti Bio) and Design Therapeutics. In addition, we compete with other companies who are focused on developing and commercializing rare disease therapies, including Agios, Alexion, Amicus, BioCryst, Biomarin, Ultragenyx, and others who may develop products that could compete with CTI-1601, or other rare disease therapies that we may target and develop.

Many of our competitors have significantly greater financial, technical and human resources than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated amongst a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop or market products or other novel therapies that are more effective, safer or less costly than our product candidates or obtain regulatory approval for their products more rapidly than we may obtain approval for our product candidates.

Intellectual Property

Our success depends in large part upon our ability to obtain and maintain proprietary protection for our current and future products and technologies, and to operate without infringing the proprietary rights of others. Our policy is to protect our proprietary position by, among other methods, filing for patent applications on inventions that are important to the development and conduct of our business with the U.S. Patent and Trademark Office and its foreign counterparts. We also intend to rely on regulatory exclusivity (also called data package exclusivity), which is separate and distinct from the protection afforded by patents, to protect our products. We further protect our proprietary information by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. Agreements with our employees also prevent them from bringing the proprietary rights of third parties to us. In addition, we require confidentiality or service agreements from third parties that receive our confidential information or materials.

As of March 1, 2021, our intellectual property portfolio was composed of numerous international and United States non-provisional applications and United States provisional patent applications that we own or co-own, and 5 issued patents and additional provisional patent applications in the United States that we license from academic institutions. The issued patents in the United States licensed by us, which include issued patents generically covering the composition of matter for CTI-1601 and methods for treating Friedreich's ataxia, have expiration dates between 2024 and 2034. The international and the United States non-provisional patent applications licensed by us relate to composition of matter and methods of use for CTI-1601.

The additional patent applications we own or co-own which include international and United States non-provisional patent applications and United States provisional patent applications are related to the development of CTI-1601 and to our peptide-delivery platform technology. If the non-provisional patent applications owned or co-owned by us result in issued patents, such patents are expected to expire between 2040 and 2041, without taking potential patent term adjustment or patent term extension into consideration.

A provisional patent application allows for an effective filing date to be established with regard to an invention, but once a provisional patent application is filed, either a corresponding non-provisional patent application or a petition to convert the provisional patent application into a non-provisional patent application must be filed within 12 months or such effective filing date will be lost. If we or our licensor timely files non-provisional patent applications in the United States and in countries outside of the United States with regard to our provisional patent applications and these non-provisional patent applications result in issued patents, such patents are expected to expire in 2041, without taking potential patent term adjustment or patent term extension into consideration.

CTI-1601 is covered by licensed issued patents (composition of matter and methods of use) in the United States which, if properly maintained, will expire in 2024 and 2025 (respectively), excluding any patent term extensions that might be available following the grant of marketing authorizations. We also possess an exclusive license to an international and a United States non-provisional patent application for CTI-1601 (composition of matter and methods of use). If the international patent applications are timely nationalized in countries outside of the United States, and the patent applications in the United States and other countries result in issued patents, those patents would be expected to expire in the United States and in countries outside of the United States in 2040, This estimated expiration excludes any patent term adjustment that might be available following the grant of the patent and any patent term extensions that might be available following the grant of marketing authorizations. We cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We also use other forms of protection besides patent protection and regulatory exclusivity, such as trademark, copyright, and trade secret protection, to enhance our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable. We aim to take advantage of all of the intellectual property rights that are available to us and believe that this comprehensive approach will provide us with proprietary exclusive positions for our product candidates, such as CTI-1601, where available.

In-License Agreements

We are party to a License Agreement (the "WFUHS License"), dated November 30, 2016 with Wake Forest University Health Sciences ("WFUHS") and a License Agreement (the "IU License"), dated November 30, 2016, as amended, with Indiana University ("IU"). Such agreements provide for a transferable, worldwide license to certain patent rights regarding technology used by us with respect to the development of CTI-1601.

In partial consideration for the right and license granted under these agreements, we will pay each of WFUHS and IU a royalty of a low single digit percentage of net sales of licensed products depending on whether there is a valid patent covering such products. As additional consideration for these agreements, we are obligated to pay each of WFUHS and IU certain milestone payments of up to $2.6 million in the aggregate upon the achievement of certain developmental milestones, commencing on the enrollment of the first patient in a Phase 1 clinical trial. We will also pay each of WFUHS and IU sublicensing fees ranging up to a low double-digit percentage of sublicense consideration depending on our achievement of certain regulatory milestones as of the time of receipt of the sublicense consideration. We are also obligated to reimburse WFUHS and IU for patent-related expenses. In the event that we dispute the validity of any of the licensed patents, the royalty rate would be tripled during such dispute. We are also obligated to pay to IU a minimum annual royalty of less than $0.1 million per annum starting in the 2020 calendar year for the term of the agreement.

In the event that we are required to pay IU consideration, then we may deduct 20% of such IU consideration on a dollar-for-dollar basis from the consideration due to WFUHS. In the event that the Company is required to pay WFUHS consideration, then we may deduct 60% of such WFUHS consideration on a dollar-for-dollar basis from the consideration due to IU.

During the twelve months ended December 31, 2020 and 2019, no milestones were achieved, and no expense was recognized. Both agreements continue from their effective date through the last to expire of the licensed patents unless earlier terminated by either party.

Manufacturing and Supply

CTI-1601 is a biologic fusion protein that is produced in E. coli. We have worked with contract manufacturers to develop a cGMP manufacturing process and analytical methods for drug substance to support Phase 1 clinical trials. Drug product was also developed and packaged into single use vials for the Phase 1 clinical program. We also use third party manufacturers for the production of drug product, clinical packaging and storage and distribution. We relied on third parties to store the CTI-1601 master cell bank and working cell bank, each stored at a different location. We continue to advance the manufacturing of CTI-1601, obtain stability data, and produce drug product for ongoing toxicology studies and future clinical trials. We are continually trying to optimize our manufacturing process to increase yields and decrease costs and increase reliability in supply chains. The final process will need to be successfully scaled up to support commercial manufacturing.

Human Capital Resources

In order to achieve the goals and expectations of our Company, it is crucial that we continue to attract and retain top talent. To facilitate talent attraction and retention, we strive to make our company a safe and rewarding workplace, with opportunities for our employees to grow and develop in their careers, supported by strong compensation, benefits and health and wellness programs, and by programs that build connections between our employees. In response to the COVID-19 pandemic, we implemented significant changes that we determined were in the best interest of our employees, and which comply with local and federal government regulations. This includes having some of our non-laboratory employees work from home, while implementing additional safety measures for employees continuing critical on-site work.

As of March 1 2021, we employed 28 full-time employees in the United States. None of our employees are represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Scientific Advisors

We have established a scientific advisory board and we regularly seek advice and input from these experienced thought leaders on matters related to our research and development programs. The members of our scientific advisory board consist of distinguished research scientists, professors and industry experts recognized as key opinion leaders in the fields of rare disease, pediatrics and mitochondrial disease. Their scientific perspectives will be invaluable to determine our strategic scientific pathway and support the development of other potential treatments for complex rare diseases to help fill unmet medical needs in this space. We intend to continue to leverage the broad expertise of our advisors by seeking their counsel on important topics relating to our product development and clinical development programs. Our scientific advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. All of our scientific advisors are affiliated with other entities and devote only a small portion of their time to us.

Our scientific advisors are set forth in the table below:

Name	Title
Rusty Clayton, DO	Consultant, Scientific Advisory Board Chair
Marni Joy Falk, MD	Executive Director, Mitochondrial Medicine Frontier Program at Children's Hospital of Philadelphia; Professor, Department of Human Genetics and Department of Pediatrics, University of Pennsylvania Perelman School of Medicine
Giovanni Manfredi, MD, PhD	Finbar and Marianne Kenny Professor of Clinical and Research Neurology, Weill Cornell Medicine; Professor of Neuroscience, Weil Cornell Medicine
Mark Payne, MD	Professor of Pediatrics, Indiana University School of Medicine
Marshall Summar, MD	Margaret O'Malley Chair of Genetic Medicine at Children's National Hospital; Chair, Division of Genetics of Metabolism and Director, Rare Disease Institute, Children's National Hospital

Facilities

We lease office and laboratory space, which consists of approximately 5,000 square feet and 1,750 square feet located in Bala Cynwyd, PA and Philadelphia, PA, respectively. Our office lease expires in August 2023 with an option to extend for three years, and our laboratory lease expires in December 2021, with an option to extend for an additional year. The Company believes that it will need to increase both its office and laboratory facilities in the near
term. We believe that both appropriate office and laboratory space will be readily available on commercially reasonable terms.

As part of the Merger (as defined below) with Zafgen, Inc., we acquired a non-cancellable operating lease for approximately 17,705 square feet of office space at 3 Center Plaza, Boston, Massachusetts, or the Boston Lease. The Boston Lease expires on October 30, 2029. On October 27, 2020, we entered into a sublease agreement whereby we subleased all 17,705 square feet of office space leased under the Boston Lease until October 30, 2029.

Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, if determined adversely to us, would individually or taken together have a material adverse effect on us.

Corporate Information

We were founded in 2005 as a Delaware corporation under the name Zafgen, Inc., or Zafgen. On May 28, 2020, Zafgen completed a reverse merger with Chondrial Therapeutics, Inc., or Chondrial, in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated December 17, 2019, by and among Zafgen, Zordich Merger Sub, Inc., Chondrial and Chondrial Therapeutics Holdings, LLC, pursuant to which Zordich Merger Sub, Inc. merged with and into Chondrial, with Chondrial surviving as a wholly owned subsidiary of the Company. Following completion of the Merger, Zafgen, Inc. changed its name to Larimar Therapeutics, Inc.

Our principal executive offices are located at Three Bala Plaza East, Suite 506, Bala Cynwyd, PA 19004, and our telephone number is (844) 511-9056. Our website address is www.larimartx.com. The information on, or that can be accessed through, our website is not part of this prospectus and is not incorporated by reference herein. We have included our website address as an inactive textual reference only.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission, or the SEC, under the Securities Exchange Act of 1934, as amended, or the Exchange Act. The SEC maintains an internet website, www.sec.gov, that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC.

Copies of each of our filings with the SEC on Form 10-K, Form 10-Q and Form 8-K and all amendments to those reports, can be viewed and downloaded free of charge at our website, www.larimartx.com as soon as reasonably practicable after the reports and amendments are electronically filed with or furnished to the SEC.

Our code of ethics, other corporate policies and procedures, and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through our website at www.larimartx.com. We intend to post information regarding any amendments to, or waivers from, our code of ethics on our website.

Government Regulation

In the United States, drug and biologic products are licensed by FDA for marketing under the Public Health Service Act, referred to as the PHS Act, and regulated under the Federal Food, Drug, and Cosmetic Act, or the FDCA. Both the FDCA and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, purity, potency, efficacy, labeling, packaging, storage, record keeping, distribution, marketing, sales, import, export, reporting, advertising and other promotional practices involving drug and biological products. FDA clearance must be obtained before clinical testing of drug and biologic products. FDA licensure also must be obtained before marketing of drug and biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Development Process

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

- completion of nonclinical laboratory tests and animal studies according to Good Laboratory Practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;

- preparation of clinical trial material in accordance with Good Manufacturing Practices, or GMPs;
- submission to the FDA of an application for an Investigational New Drug, or IND application, which must become effective before human clinical trials may begin;
- approval by an institutional review board, or IRB, reviewing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs and any additional requirements for the protection of human research subjects and their health information, to establish the safety, purity, potency, and efficacy, of the proposed drug or biological product for its intended use;
- submission to the FDA of New Drug Application, or NDA, or Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, potency, and efficacy from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection prior to NDA or BLA approval of the manufacturing facility or facilities where the drug or biological product is produced to assess compliance with GMPs, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the NDA or BLA;
- potential FDA Advisory Committee meeting to elicit expert input on critical issues and including a vote by external committee members;
- FDA review and approval, or licensure, of the NDA or BLA, and payment of associated user fees, when applicable; and
- compliance with any post approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategies, or REMS, and the potential requirement to conduct post approval studies.

Before testing any drug or biological product candidate in humans, the product candidate enters the preclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, pharmacology, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLPs.

The clinical study sponsor must submit the results of the nonclinical 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 nonclinical testing typically continues after the IND is submitted. An IND is an exemption from the FDCA that allows an unapproved product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA requests certain changes to a protocol before the trial can begin, or the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug or biological 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 recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical trials may involve the administration of the drug or biological product candidate to healthy volunteers or subjects under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials involving some products for certain diseases, including some rare diseases may begin with testing in patients with the disease. 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 or his or her legal representative provide informed consent. Further, each clinical trial must be reviewed and approved by an independent 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 study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the 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. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee.

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

- ***Phase 1***. The drug or biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for rare diseases, the initial human testing is often conducted in patients.

- ***Phase 2***. The drug or biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- ***Phase 3***. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. In drugs and biologics for rare diseases where patient populations are small and there is an urgent need for treatment, Phase 3 trials might not be required if an adequate risk/benefit can be demonstrated from the Phase 2 trial.

An Open Label Expansion study may also be conducted. An OLE study typically enrolls participants of previous clinical trials and is designed to gather the long-term safety and tolerability data on a potential new medicine beyond the time period of the original studies.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing 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 and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reactions over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or 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 drug or biological product has been associated with unexpected serious harm to patients.

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

There are also various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with the research. In each of these areas, the FDA and other regulatory authorities have broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals.

Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its 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.

U.S. Review and Approval Processes

After the completion of clinical trials of a drug or biological product, FDA approval of an NDA or BLA must be obtained before commercial marketing of the product. The NDA or BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, as amended, or PDUFA, each NDA or BLA may be accompanied by a significant user fee. Under federal law, the submission of most applications is subject to an application user fee. The sponsor of an approved application is also subject to an annual program fee. 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 NDAs or BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews an NDA or BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any NDA or BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. The application also needs to be published and submitted in an electronic format that can be processed through the FDA's electronic systems. If the electronic submission is not compatible with FDA's systems, the NDA or BLA can be refused for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA or BLA. The FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe, potent, and effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with GMPs to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel products or 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 drug or biological product approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the NDA or BLA without a REMS, if required.

Before approving an NDA or BLA, the FDA may inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical trial sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure GMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

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

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

One of the performance goals agreed to by the FDA under the PDUFA is to review standard NDAs or BLAs in 10 months from filing and priority NDAs or BLAs in six months from filing, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the NDA or BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of drug and biological products continues after approval, particularly with respect to GMP. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the GMP regulations, including quality control and quality assurance and maintenance of records and documentation.

Following approval, the manufacturing facilities are subject to biennial inspections by the FDA's and such inspections may result in an issuance of FDA Form 483 deficiency observations, untitled letter, or a warning letter, which can lead to plant shutdown and other more serious penalties and fines. Prior to the institution of any manufacturing changes, a determination needs to be made whether FDA approval is required in advance. If not done in accordance with FDA expectations, the FDA may restrict supply and may take further action. Annual product reports are required to be submitted annually. Other post-approval requirements applicable to drug and biological products, include reporting of GMP 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.

After an NDA or BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release 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 of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA may conduct laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of drug and biological products. Systems need to be put in place to record and evaluate adverse events reported by health care providers and patients and to assess product complaints. An increase in severity or new adverse events can result in labeling changes or product recall. Defects in manufacturing of commercial products can result in product recalls.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or inpatient 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. 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. 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 sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval or license revocation, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect.

Drug and biological product manufacturers and other entities involved in the manufacture and distribution of approved drug and biological products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain GMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including withdrawal of the product from the market. 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.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation (referred to as "ODD") to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. ODD must be requested before submitting a BLA. After the FDA grants ODD, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. ODD does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has ODD receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same biological product for the same indication for seven years, except in limited circumstances, such as not being able to supply the product for patients or showing clinical superiority to the product with orphan exclusivity.

Competitors, however, may receive approval of different products for the 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 product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Expedited Review and Approval Programs

The FDA has various programs, including Fast Track designation, priority review, accelerated approval, and breakthrough therapy designation, that are intended to expedite or simplify the process for the development and FDA review of drug and biological products that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drug and biological products to patients earlier than under standard FDA review procedures. To be eligible for a Fast Track designation, the FDA must determine, based on the request of a sponsor, that a drug or biological product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. 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 NDA or BLA before the application is complete, a process known as rolling review.

The FDA may give a priority review designation, such as a rare pediatric disease designation, to drug or biological products that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Most products that are eligible for Fast Track designation may also be considered appropriate to receive a priority review. In addition, drug and biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug or biological product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug or biological product receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug or biological product may be subject to accelerated withdrawal procedures.

Moreover, under the Food and Drug Administration Safety and Innovation Act enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drug and biological products designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

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 decides that the time period for FDA review or approval will not be shortened. Furthermore, fast-track designation, priority review, accelerated approval and breakthrough therapy designation, do not change the standards for approval and may not ultimately expedite the development or approval process.

Biologics Price Competition and Innovation Act

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, which was enacted as part of the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or PPACA, created an abbreviated approval pathway for biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-licensed reference biological product via an approved BLA. Biosimilarity to an approved reference product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity is demonstrated in steps beginning with rigorous analytical studies or "fingerprinting", in vitro studies, in vivo animal studies, and generally at least one clinical study, absent a waiver from the Secretary of Health and Human Services. The biosimilarity exercise tests the hypothesis that the investigational product and the reference product are the same. If at any point in the stepwise biosimilarity process a significant difference is observed, then the products are not biosimilar, and the development of a stand-alone NDA or BLA is necessary. In order to meet the higher hurdle of interchangeability, a sponsor must demonstrate that the biosimilar product can be expected to produce the same clinical result as the reference product, and for a product that is administered more than once, that the risk of switching between the reference product and biosimilar product is not greater than the risk of maintaining the patient on the reference product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being evaluated by the FDA. Under the BPCIA, a reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product.

Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing clinical studies, commercial sales, and distribution of our products. Most countries outside of the United States require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the U.S. before we can commence clinical studies or marketing of the product in those countries. The approval process and requirements vary from country to country, so the number and type of nonclinical, clinical, and manufacturing studies needed may differ, and the time may be longer or shorter than that required for FDA approval.

To obtain regulatory approval of an orphan drug under the EU regulatory system, we are mandated to submit a Marketing Authorization Application, or MAAs, to be assessed in the Centralized Procedure. The centralized procedure, which came into operation in 1995, allows applicants to obtain a marketing authorization that is valid throughout the EU. It is compulsory for medicinal products manufactured using biotechnological processes, for orphan medicinal products and for human products containing a new active substance which was not authorized in the Community before 20 May 2004 (date of entry into force of Regulation (EC) No 726/2004) and which are intended for the treatment of AIDS, cancer, neurodegenerative disorder or diabetes. The centralized procedure is optional for any other products containing new active substances not authorized in the Community before 20 May 2004 or for products which constitute a significant therapeutic, scientific or technical innovation or for which a Community authorization is in the interests of patients at Community level. When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the European Medicines Agency, or EMA, to be assessed by the Committee for Medicinal Products for Human Use, or CHMP. The CHMP is responsible for conducting the assessment of whether a medicine meets the required quality, safety and efficacy requirements, and whether the product has a positive risk/benefit/risk profile. The procedure results in a Commission decision, which is valid in all EU Member States. Centrally authorized products may be marketed in all Member States. Centralized procedure: Full copies of the MA application are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's scientific assessment of the medicinal product and prepare draft reports. Once the draft reports are prepared (other experts might be called upon for this purpose), they are sent to the CHMP, whose comments or objections are communicated to the applicant. The rapporteur is therefore the privileged interlocutor of the applicant and continues to play this role, even after the MA has been granted.

The rapporteur and co-rapporteur then assess the applicant's replies, submit them for discussion to the CHMP and, taking into account the conclusions of this debate, prepare a final assessment report. Once the evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the authorization. When the opinion is favorable, it shall include the draft summary of the product's characteristics, the package leaflet and the texts proposed for the various packaging materials. The time limit for the evaluation procedure is 210 days. The EMA then has fifteen days to forward its opinion to the Commission. This is the start of the second phase of the procedure: the decision-making process. The Agency sends to the Commission its opinion and assessment report, together with annexes containing: the SmPC, or Annex 1; the particulars of the MAH responsible for batch release, the particulars of the manufacturer of the active substance and the conditions of the marketing authorization, or Annex 2; and the labelling and the package leaflet, or Annex 3. The annexes are translated into the 22 other official languages of the EU During the decision-making process, the Commission services verify that the marketing authorization complies with Union law. The Commission has fifteen days to prepare a draft decision. The medicinal product is assigned a Community registration number, which will be placed on its packaging if the marketing authorization is granted. During this period, various Commission directorates-general are consulted on the draft marketing authorization decision.

The draft decision is then sent to the Standing Committee on Medicinal Products for Human Use, (Member States have one representative each in both of these committees) for their opinions. The Centralized Procedure provides for the grant of a single marketing authorization that is valid for all EU member states. The Decentralized Procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

Applications from persons or companies seeking "orphan medicinal product designation" for products they intend to develop for the diagnosis, prevention, or treatment of life-threatening or very serious conditions that affect not more than 5 in 10,000 persons in the EU are reviewed by the Committee for Orphan Medicinal Products, or COMP. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating, or serious and chronic condition in the EU and that without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the EU of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. We have obtained orphan drug designation for CTX-1601.

Orphan drug designation provides opportunities for fee reductions, protocol assistance and access to the centralized procedure before and during the first year after marketing approval. Fee reductions are not limited to the first year after marketing approval for small and medium enterprises. In addition, if a product which has an orphan drug designation subsequently receives EMA marketing approval for the indication for which it has such designation, the product is entitled to orphan market exclusivity, which means the EMA may not approve any other application to market a similar drug for the same indication for a period of 10 years. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Competitors may receive marketing approval of different drugs or biologics for the indications for which the orphan product has exclusivity. In order to do so, however, they must demonstrate that the new drugs or biologics are clinically superior to the existing orphan product. This demonstration of clinical superiority may be done at the time of initial approval or in post-approval studies, depending on the type of marketing authorization granted.

A Pediatric Investigation Plan, or PIP, in the EU is aimed at ensuring that the necessary data are obtained to support the authorization of a medicine for children, through studies in children. All applications for marketing authorization for new medicines have to include the results of studies as described in an agreed PIP, unless the study results are deferred, or the medicine is exempt because of a waiver. This requirement also applies when a marketing-authorization holder wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized and covered by intellectual property rights. Several rewards and incentives for the development of pediatric medicines for children are available in the E.U. Medicines authorized across the E.U. with the results of studies from a PIP included in the product information are eligible for an extension of their supplementary protection certificate by six months. This is the case even when the studies' results are negative. For orphan medicines, the incentive is an additional two years of market exclusivity. Scientific advice and protocol assistance at the Agency are free of charge for questions relating to the development of pediatric medicines.

The U.K. left the EU on January 31, 2020 following which, existing EU medicinal product legislation continued to apply in the U.K. during the transition period under the terms of the EU-UK Withdrawal Agreement. A transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the U.K. and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, and became effective on the January 1, 2021.

From January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, will be the U.K.'s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales and Scotland (together Great Britain, or GB); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a draft guidance on how various aspects of the U.K. regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, marketing authorizations, importing, exporting and pharmacovigilance and is relevant to any business involved in the research, development or commercialization of medicines in the U.K. The new guidance will be given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the Exit Regulations. The U.K. regulatory regime largely mirrors that of the EU.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing E.U. MAs for centrally authorized products will automatically be converted (grand fathered) into U.K. MAs free-of-charge on January 1, 2021.

There will be no pre-marketing authorization orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the GB market, i.e., the prevalence of the condition in GB (rather than the EU) must not be more than 5 in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB or EU/European Economic Area, wherever is earliest.

Healthcare Laws and Regulations

Sales of our product candidate, if approved, or any other future product candidate will be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we might conduct our business. The healthcare laws and regulations that may affect our ability to operate include the following:

- The federal Anti-Kickback Statute makes it illegal for any person or entity to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is in exchange for or to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value;

- Federal false claims and false statement laws, including the federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent;

- HIPAA created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors or making any false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their implementing regulations, impose obligations on certain types of individuals and

- entities regarding the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information;

- The federal Physician Payments Sunshine Act 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 CMS information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- The Foreign Corrupt Practices Act, or FCPA prohibits U.S. businesses and their representatives from offering to pay, paying, promising to pay or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business.

Many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government's and/or pharmaceutical industry's voluntary compliance guidelines, 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, as well as state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA. Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

Healthcare Reform

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The United States government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. In recent years, Congress has considered reductions in Medicare reimbursement levels for drugs administered by physicians. CMS, the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payers.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act is intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers, and impose additional health policy reforms. Among other things, the Affordable Care Act expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum Medicaid rebate for both branded and generic drugs, expanded the 340B program, and revised the definition of average manufacturer price, or AMP, which could increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also extended Medicaid drug rebates, previously due only on fee-for-service Medicaid utilization, to include the utilization of Medicaid managed care organizations as well and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the amount of rebates due on those drugs. On February 1, 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate program under the Affordable Care Act. These regulations became effective on April 1, 2016. Since that time, there have been significant ongoing efforts to modify or eliminate the Affordable Care Act. On January 20, 2017, President Trump signed an executive order directing federal agencies to exercise existing authorities to reduce burdens associated with the Affordable Care Act pending further action by Congress. In October 2017, he signed an Executive Order which directed federal agencies to modify how the Affordable Care Act is implemented. The Tax Act, enacted on December 22, 2017, repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, as amended, or the Code, commonly referred to as the individual mandate,

Other legislative changes have been proposed and adopted since the passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than $1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further legislative and regulatory changes under the Affordable Care Act remain possible, although the new Administration under President Biden has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. President Biden indicated that he intends to use executive orders to undo changes to the Affordable Care Act made by the former administration and would advocate for legislation to build on the Affordable Care Act. It is unknown what form any such changes or any law would take, and how or whether it may affect our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

The Affordable Care Act has been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court which heard oral arguments in the case on November 10, 2020. A ruling is expected in 2021.

The Affordable Care Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each individual pharmaceutical manufacturer pays a prorated share of the branded prescription drug fee, based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. Furthermore, the law requires manufacturers to provide a 50% discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the "donut hole." The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole," by increasing from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

The Affordable Care Act also expanded the Public Health Service's 340B drug pricing program. The 340B drug pricing program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. The Affordable Care Act expanded the 340B program to include additional types of covered entities: certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, each as defined by the Affordable Care Act. Because the 340B ceiling price is determined based on AMP and Medicaid drug rebate data, revisions to the Medicaid rebate formula and AMP definition could cause the required 340B discounts to increase. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives as well. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed, and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for pharmaceutical products.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

ITEM 1A. RISK FACTORS

You should consider carefully the following risks and uncertainties when reading this Annual Report. If any of the following risks occur our business, financial condition and results of operations could be materially and adversely Although we believe that we have identified and discussed below the key risk factors affecting our business, there may be additional risks and uncertainties that are not presently known or that are not currently believed to be significant that may adversely affect our performance or financial condition. affected. In that event, the trading price of our common stock could decline.

Risks Related to Our Financial Position and Need for Capital

We have incurred significant losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

Since our inception we have devoted substantially all of our resources to the development of CTI-1601. We have incurred significant losses in each year of operation since our inception in 2016. For the year ended December 31, 2020, we had net losses of $42.5 million and as of December 31, 2020, had an accumulated deficit of $65.6 million and we expect to continue to incur significant expenses and net operating losses for the foreseeable future.

We have devoted substantially all of our financial resources and efforts to research and development, including nonclinical studies, our clinical development program, the development of manufacturing processes as well as the manufacture of initial lots of clinical trial material. We expect to incur significant losses for the foreseeable future to further develop and commercialize our lead drug candidate.

We expect that our expenses will increase substantially if and as we:

- continue clinical development efforts for CTI-1601;
- seek regulatory and marketing approvals in the United States and in foreign jurisdictions for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure to commercialize various products for which we may obtain marketing approval, if any;
- contract for the manufacture of larger quantities of product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio; and
- hire and retain additional personnel, such as clinical, manufacturing, quality control, regulatory, finance, and compliance personnel.

Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholder’s (deficit) equity and working capital.

We have no commercial revenue and may never become profitable.

To date, we have not generated any commercial revenue. Our ability to generate revenue and become profitable depends upon our ability to obtain regulatory approval for, and successfully commercialize, CTI-1601 or other product candidates that we may develop, in-license or acquire in the future.

This will require success in a range of challenging activities, including completing numerous clinical trials of CTI-1601 or any future product candidates, obtaining marketing approval for CTI-1601 and any future product candidates, manufacturing, marketing and selling those products for which we, or any future collaborators or partners, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Even if we are able to successfully achieve the above, we do not know what the reimbursement status of CTI-1601 or any other future product candidates will be or when any of these products will generate revenue for us, if at all. We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, nonclinical studies and clinical trials and the regulatory approval process for CTI-1601 and any future product candidates.

Our ability to generate revenue from CTI-1601 or any future product candidates also depends on a number of additional factors, including our ability to:

- successfully complete development activities, including the remaining nonclinical studies and planned clinical trials for our product candidates;
- complete and submit New Drug Applications, or NDAs, and Biologics License Applications, or BLAs, to the U.S. Food and Drug Administration, or FDA, and Marketing Authorization Applications, or MAAs, to the European Medicines Agency, or EMA, and obtain regulatory approval for indications for which there is a commercial market;
- complete and submit applications to, and obtain regulatory approval from, other foreign regulatory authorities;
- manufacture or have manufactured any approved products in commercial quantities and on commercially reasonable terms;
- develop a commercial organization, or find suitable partners, to market, sell and distribute approved products in the markets in which we have retained commercialization rights;
- achieve acceptance among patients, clinicians and advocacy groups for any products we develop;
- obtain coverage and adequate reimbursement from third parties, including government payors; and
- set a commercially viable price for any products for which we may receive approval.

Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of increased expenses, and if or when we might achieve or maintain profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we are able to complete the processes described above, we anticipate incurring significant costs associated with commercializing CTI-1601 or any of our future product candidates. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We need to raise additional funding. This funding may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed would force us to delay, limit or terminate our product development efforts or other operations.

We expect to continue to spend substantial and increasing amounts to conduct clinical trials of CTI-1601 and further research and development activities for CTI-1601, and for any additional product candidates that we may develop, in-license or acquire in the future. In addition, raising funds in the current economic environment may present substantial challenges, and our expenses will increase as we expand, through development, in-license or acquisition, our pipeline of product candidates. If we obtain marketing approval for any of our product candidates, we will likely incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. Accordingly, we will need to obtain additional funding in connection with our continuing operations.

As of December 31, 2020, our existing cash, cash equivalents and marketable debt securities were $92.6 million, excluding restricted cash of $1.3 million. This amount will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of CTI-1601. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. 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. 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. 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, or on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs, the manufacture of clinical and commercial supplies or the commercialization of any product candidate. Our failure to raise capital as and when needed would have a negative impact on our business, financial condition and results of operations and our ability to pursue the development of CTI-1601 or future product candidates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies, CTI-1601 or other product candidates that we may develop, in-license or acquire in the future.

We may seek additional capital through a combination of private or public equity offerings, debt financings, collaborations and licensing arrangements or other sources. To the extent we raise additional capital through the sale of equity or convertible debt securities, existing ownership interests will be diluted and the terms of such financings may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt or equity financings may be coupled with an additional equity component, such as warrants to purchase shares, which could also result in dilution of our existing stockholder's ownership.

If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights, including future revenue streams, to CTI-1601 or other product candidates that we may develop, in-license or acquire in the future, or grant licenses on terms that are not favorable to us.

Our ability to use our NOLs and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change Net Operating Losses, or NOLs and other pre-change tax attributes (such as capitalized research and development costs and research tax credits) to offset its post-change income may be limited. We believe that as a result of our merger with Zafgen, Inc., our ability to utilize NOLs acquired in this transaction is expected to be severely limited by Section 382 of the Code. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. The Tax Cuts and Jobs Act of 2017, or Tax Act, which significantly reformed the Code, also reduced the corporate income tax rate to 21%, from a prior rate of 35%. This may cause a reduction in the economic benefit of our NOLs and other deferred tax assets available to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed and would adversely affect our business, financial condition and results of operations.

Risks Related to Our Product Development and Regulatory Approvals

Our success is currently dependent upon the success of our sole product candidate, CTI-1601, which is currently in Phase 1 clinical trials. We cannot be certain that we will be successful with our clinical development or that we will be able to obtain regulatory approval for CTI-1601.

We currently have no drug products for sale and our business is currently wholly dependent on our successful clinical development, regulatory approval and commercialization of CTI-1601, which is currently completing Phase 1 clinical trials.

If our efforts to develop and commercialize CTI-1601 for the treatment of Friedreich's ataxia are unsuccessful, or we experience significant delays in doing so, our business could also be substantially harmed. The success of CTI-1601 will depend on several factors, including the following:

- maintaining our IND application with the FDA in order to continue to conduct clinical trials in the United States;
- successfully recruiting, enrolling and retaining patients in and completing our Phase 1 clinical trials and any clinical trials we may conduct in the future; including trials in pediatric patients;
- demonstrating safety, tolerability and efficacy profiles that are satisfactory to the FDA, EMA and other comparable regulatory authorities for marketing approval;
- successfully completing all necessary toxicology studies to support clinical development and regulatory approval for CTI-1601;
- receiving timely marketing approvals from applicable regulatory authorities;
- managing the extent and cost of any required post-marketing approval commitments to applicable regulatory authorities;
- establishing and maintaining arrangements with third-party manufacturers for CTI-1601, including developing, validating and maintaining a commercially viable manufacturing process that is compliant with cGMPs;
- obtaining, maintaining and protecting our patents, trade secrets and regulatory exclusivity in the United States and other countries;
- successfully launching commercial sales following any marketing approval, including establishing a specialty sales organization, or successfully partnering with another organization, if applicable;
- obtaining commercial acceptance of our products, if approved, by patients, the medical community and third-party payors and obtaining and maintaining healthcare coverage and adequate reimbursement;
- maintaining an acceptable safety profile following any marketing approval; and
- competing with other therapies.

Many of these factors are outside of our control, including the clinical development and regulatory approval processes, results of nonclinical and toxicology studies and clinical trials, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts, respectively. The process of obtaining regulatory approval is expensive and time consuming. The FDA and foreign regulatory authorities may never approve CTI-1601 for sale and marketing, and even if CTI-1601 is ultimately approved, regulatory approval may be delayed or limited in the United States or in other jurisdictions. Even if we are authorized to sell and market CTI-1601 in one or

more markets, there is no assurance that we will be able to successfully market CTI-1601 or that CTI-1601 will achieve market acceptance sufficient to generate profits. If we are unable to successfully develop and commercialize CTI-1601 due to failure to obtain regulatory approval for CTI-1601, to successfully market CTI-1601, to generate profits from the sale of CTI-1601, or due to other risk factors outlined in this report, it would have material adverse effects on our business, financial condition, and results of operations as CTI-1601 is currently our sole product candidate.

Clinical development is a lengthy and expensive process with an uncertain outcome, and the results of nonclinical studies, toxicology studies or clinical trials may not be predictive of future nonclinical studies, toxicology studies or clinical trial results.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any nonclinical studies, toxicology studies or clinical trials will be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the nonclinical study, toxicology study or clinical trial process. Despite promising nonclinical, toxicology or clinical results, any product candidate can unexpectedly fail at any stage of nonclinical, toxicology or clinical development. The historical failure rate for product candidates in our industry is high, especially for products in early stages of development.

The results from nonclinical studies, toxicology studies or clinical trials of a product candidate may not predict the results of later nonclinical or clinical trials of the product candidate, or in clinical trials with different patient populations such as children and adolescents and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through nonclinical studies and initial clinical trials. It is not uncommon to observe results in clinical trials that are unexpected based on nonclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. Favorable safety and efficacy outcomes in adult clinical trials may not be seen in pediatric clinical trials.

Moreover, current and future nonclinical and clinical data may be susceptible to varying interpretations and analyses. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. Furthermore, we cannot provide assurance that we will be able to successfully progress any future nonclinical programs from candidate identification to Phase 1 clinical development. As is typical in candidate development, we have a program of ongoing toxicology studies in animals for CTI-1601 and cannot provide assurance that the findings from such studies or any ongoing or future clinical trials will not adversely affect the clinical development of CTI-1601. For the foregoing reasons, we cannot be certain that our ongoing and planned nonclinical studies and clinical trials will be successful. If nonclinical or clinical trials for CT1-1601 or any future product candidates or indications fail to demonstrate safety or efficacy to the satisfaction of the FDA or the equivalent regulatory authorities in other countries, the FDA or equivalent regulatory authority will not approve our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition results of operations and prospects.

We do not know whether any ongoing or future clinical trials for CTI-1601 will be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed, prevented or terminated for a number of reasons, including as a result of safety concerns, or ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, other regulatory authorities, the institutional review boards, or IRBs, or ethics committees, a data monitoring committee, or safety review committee, overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA, the EMA, or other applicable regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a partial clinical hold or a full clinical hold;

- unforeseen safety issues, including any that could be identified in our prior or ongoing toxicology studies, adverse events or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials;
- lack of adequate funding to continue the clinical trial;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, such as pediatric patients, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications, and the ongoing effects of COVID-19;
- difficulties in retaining or recruiting clinical investigators in our ongoing or future clinical trials;
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, perceived lack of efficacy, side effects, screening and monitoring measures, personal issues or loss of interest;
- severe or unexpected drug-related adverse events experienced by patients in clinical trials;
- the FDA, the EMA, or other applicable regulatory authorities may disagree with our clinical trial designs, our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials; and
- reports from nonclinical studies or clinical testing of other therapies that raise safety or efficacy concerns.

Failures or delays in the completion of our clinical trials could result in increased costs and could delay, prevent or limit our ability to generate revenue and continue our business.

Our lead product candidate CTI-1601 is currently in Phase 1 clinical trials, and there are a number of FDA regulatory requirements that we must satisfy before we can commence late-stage clinical trials of CTI-1601. To receive approval of CTI-1601 in other countries we will also have to satisfy their regulatory requirements. Satisfaction of these requirements will entail substantial time, effort and financial resources. We may never satisfy these requirements. Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results or events outside of our control. The pandemic resulted in the temporary stoppage of our Phase 1 clinical trials studying CTI-1601in patients with Friedreich's ataxia. after the completion of two cohorts, In July 2020, we resumed our Phase 1 clinical trials of CTI-1601. We are conducting the clinical trial at one clinical trial site in New Jersey. Because Friedreich's ataxia is a rare disease, there are a limited number of patients in close proximity to the clinical trial site and clinical trial patients travel from throughout the United States to the clinical trial site to participate. The travel advisories and risk of infection related to COVID-19 have presented increased risks to patients traveling to our clinical trial site for dosing. While top line results from the SAD and MAD clinical trials were originally expected by the end of 2020, the delay in the clinical trial timeline caused by the ongoing impact of COVID-19 has resulted in top line results being delayed until the second quarter of 2021. If Phase 1 clinical trials of CTI-1601 fail or further delays occur, we may not be able to develop and commercialize CTI-1601 and could fail to realize the potential advantages of doing so, and it could materially adversely affect our business, financial condition and results of operations.

We may not be successful in our efforts to identify, discover or acquire additional product candidates.

We currently only have one product candidate CTI-1601, which is completing Phase 1 clinical trials in the United States. Therefore, the success of our business largely depends upon our ability to identify, develop, in-license or acquire and commercialize products targeting rare diseases. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. In addition, our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

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

We have no marketed proprietary products and have not yet advanced a product candidate beyond Phase 1 clinical trials, which makes it difficult to assess our ability to develop CTI-1601 or any future product candidates and commercialize any resulting products independently.

We have no experience in later stage clinical development, and related regulatory requirements or the commercialization of products. As a result, we have not yet demonstrated our ability to independently and repeatedly conduct clinical development after Phase 1, which has not yet been successfully completed, successfully conduct an international multi-center clinical trial, conduct a pivotal clinical trial, obtain regulatory approval, manufacture drug product on a commercial scale or arrange for a third party to do so on our behalf, and commercialize therapeutic products. We will need to develop such abilities if we are to execute on our business strategy to develop and independently commercialize product candidates for orphan and niche indications. To execute on our business plan for the development of independent programs, we will need to successfully:

- execute our clinical development plans for later-stage product candidates;
- obtain required regulatory approvals in each jurisdiction in which we will seek to commercialize products;
- build and maintain appropriate sales, distribution and marketing capabilities;
- gain market acceptance for our future products, if any; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization activities.

If we are unsuccessful in accomplishing these objectives, we will not be able to develop and commercialize any product candidates independently and could fail to realize the potential advantages of doing so, and it would materially adversely affect our business, financial condition and results of operations.

We cannot be certain that we will be able to successfully complete clinical trials for CTI-1601 or any other product candidates.

We currently have only one product candidate in clinical development, CTI-1601, which is currently completing Phase 1 clinical trials in the United States. Our business currently depends primarily on CTI-1601's successful clinical development, regulatory approval and commercialization. We submitted our IND, and our application has gone into effect, permitting the conduct of clinical trials. However, the outcome of toxicology studies and early clinical trials may not be positive and may not be predictive of the success of later nonclinical studies or clinical trials, and interim results of clinical trials do not necessarily predict success in those or future clinical trials. Success in adult clinical trials may not predict the outcome of pediatric clinical trials.

Published clinical data or case reports from third parties or early clinical trial data of CTI-1601 or any future product candidates may not be predictive of the results of later-stage clinical trials. Interpretation of results from early, usually smaller, studies that suggest a clinically meaningful response in some patients, requires caution. Results from later stages of clinical trials enrolling more patients, or different patient populations, such as pediatric patients, may fail to show the desired safety or efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), different patient population, number of patients, patient selection criteria, trial duration, drug dosage and formulation and lack of statistical power. These uncertainties are enhanced where the diseases under study lack established clinical endpoints, validated measures of efficacy, as is often the case with orphan diseases for which no drugs have been developed previously and where the product candidates target novel mechanisms. For example, to our knowledge, CTI-1601 is the only protein replacement therapy being developed for the treatment of Friedreich's ataxia and therefore nonclinical studies may not be adequate to predict efficacy in a clinical trial due to our novel protein replacement therapy platform.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, such as pediatric patients, variability of the disease being studied, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to ultimately receive positive results in clinical trials of CTI-1601, the development timeline and regulatory approval and commercialization prospects for CTI-1601, and, correspondingly, our business, financial prospects and results of operation would be negatively impacted.

Further, CTI-1601 or any future product candidates may not be approved even if they achieve their primary endpoint in clinical trials. The FDA, EMA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from nonclinical studies and clinical trials. In addition, any of these regulatory authorities may change its requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that, if successful, would potentially form the basis for an application for approval by the FDA, EMA or another regulatory authority. Furthermore, any of these regulatory authorities may also approve CTI-1601 or any future product candidates for a narrower indication than we may request or may grant approval contingent on the performance of costly post-marketing clinical trials. Any of the above could materially adversely affect our business, financial condition and results of operations.

We may experience difficulties identifying and enrolling patients in our clinical trials given the limited number of patients who have the disease for which CTI-1601 is being studied or for any other product candidate we may study in the future. Difficulty in enrolling patients could delay or prevent clinical trials of CTI-1601 or any future product candidate.

Identifying and qualifying patients to participate in clinical trials of CTI-1601 is critical to our success. The timing of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing CTI-1601, and we may experience delays in our clinical trials if we encounter difficulties in enrollment, such as difficulties with enrollment in pediatric clinical trials.

The conditions for which we are planning to evaluate CTI-1601 and any product candidates we may evaluate in the future, are rare genetic diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. We are investigating our product candidate in Friedreich's ataxia, a rare disease. Arranging for investigative sites and recruiting patients for clinical trials in this disease may be very difficult. In addition, if other companies are investigating their investigational products in Friedreich's ataxia, it may be more difficult to enroll eligible patients into our clinical trials.

In addition to the rarity of Friedreich's ataxia and other diseases that we are studying, the eligibility criteria of our clinical trials will further limit the pool of available study participants as it will require patients to have specific characteristics that we can measure to assure their disease is either severe enough or not too advanced to include them in a clinical trial. The process of finding and diagnosing patients may prove costly, especially since the diseases we are studying are rare. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical trials because of demographic criteria for prospective patients, the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical trial sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical trials can also adversely impact enrollment. Furthermore, our inability to enroll a sufficient number of patients for our clinical trials, including pediatric clinical trials, could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for CTI-1601 or any future product candidates, and jeopardize our ability to achieve our clinical development timeline and goals, including the dates by which we will commence, complete and receive results from clinical trials. If patients are unwilling to participate in our trials for any reason, the timeline for recruiting patients, conducting trials, and obtaining regulatory approval of potential products may be delayed, Enrollment delays in our clinical trials may also jeopardize our ability to commence sales of and generate revenues from CTI-1601, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Friedreich's ataxia has no FDA-approved treatments, and clinical endpoints required to obtain approval are not well defined.

There are currently no therapies approved to treat Friedreich's ataxia. We have concentrated our research and development efforts on developing a novel therapeutic for the treatment of Friedreich's ataxia, and our future success depends on the success of this therapeutic approach. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. Given the nature of Friedreich's ataxia, we may have to devise novel clinical endpoints to be tested in our clinical trials, which can lead to some subjectivity in interpreting trial results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore denying approval, which would materially adversely affect our business, financial condition and results of operations. As a result, the design and conduct of clinical trials for a therapeutic product candidate such as CTI-1601 that is intended to deliver human FXN through a subcutaneously administered, recombinant fusion protein in Friedreich's ataxia patients are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of CTI-1601 in Friedreich's ataxia because of the limited clinical experience with our mechanism of action in these patients.

In particular, regulatory authorities in the United States and the European Union, or the EU, have not issued definitive guidance as to how to measure and achieve efficacy in treatments for Friedreich's ataxia. As a result, the design and conduct of clinical trials of CTI-1601 may take longer, be more costly or be less effective as part of the novelty of development in Friedreich's ataxia. We may use new or novel endpoints or methodologies, and the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results. Even if applicable regulatory authorities do not object to our proposed endpoints in an earlier stage clinical trial, such regulatory authorities may require evaluation of additional or different clinical endpoints in later-stage clinical trials.

CTI-1601 may cause adverse events or undesirable side effects that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

We are collecting data about CTI-1601 from ongoing Phase 1 clinical trials and toxicology studies and any adverse events or undesirable side effects caused by, or other unexpected properties of, CTI-1601 could cause us, any future collaborators, an IRB or ethics committee or regulatory authorities to interrupt, delay or halt clinical trials of our product candidate and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. It is possible that as we progress CTI-1601 through clinical trials and toxicology studies, or as the use of CTI-1601 becomes more widespread if it receives regulatory approval, illnesses, injuries, discomforts and other adverse events that were not observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, may be reported by patients. If such side effects become known later in development or after approval, such findings may harm our business, financial condition and prospects significantly. Further, if a serious safety issue is identified in connection with the use of CTI-1601 commercially or in third-party clinical trials elsewhere, such issues may adversely affect the development potential of CTI-1601 elsewhere or result in regulatory authorities restricting our ability to develop or commercialize CTI-1601.

Further, if CTI-1601 were to receive marketing approval and we or others identify undesirable side effects caused by the product (or any other product) after the approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may request that we recall or withdraw the product from the market or may limit the approval of the product through labeling or other means;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication or a precaution, or labeling restrictions based on patient population;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we may decide to recall or remove the product from the marketplace;
- we could be sued and/or held liable for injury caused to individuals exposed to or taking our product candidates;
- damage to the public perception of the safety of CTI-1601; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues, all of which would materially adversely affect our business, financial condition and results of operations.

Our approach to discover and develop fusion proteins for delivering proteins is novel and may never lead to marketable products.

We have concentrated our efforts and research and development activities on delivering proteins (FXN or other) to intracellular targets. Our future success depends on the successful development and manufacturing of such therapeutics and the effectiveness of our platform. The scientific discoveries that form the basis for our research are relatively new.

CTI-1601 uses a novel and unproven approach and mechanism to treat Friedreich’s ataxia and therefore its efficacy and safety are difficult to predict, and there is no guarantee that CTI-1601 will be approved by the FDA, the EMA, or any other regulatory authorities.

If CTI-1601 proves to be ineffective, unsafe or commercially unviable, it is possible that our platform and pipeline would have little, if any, value, which would substantially harm our business, financial condition, results of operations and prospects. In addition, our approach may expose us to additional financial risks and make it more difficult to raise additional capital than other, more advanced proven technologies, which would materially adversely affect our business, financial condition and results of operations.

Protein replacement therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our protein replacement therapy platform or product candidates or otherwise harm our business.

The manufacture of fusion proteins, such as CTI-1601 and any fusion protein candidates, is technically complex and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events may delay the availability of material for clinical trials and commercial products for CTI-1601 or any fusion protein product that may receive regulatory approval in the future. Additionally, because biologic products are complex, the manufacture of such products and product candidates is more difficult and costly. We may not be able to have such products reliably manufactured in accordance with the applicable regulatory requirements in sufficient quantities to support our development programs and, if ultimately approved, commercial supply. We currently contract with third parties for the manufacturing of program materials for CTI-1601.

There are a limited number of contract manufacturers who specialize in the manufacture of biologic products and those that do may still be developing appropriate processes, controls and facilities for large-scale production. While we believe that there will be sufficient sources of supply that can satisfy our clinical and commercial requirements, we cannot be certain that we will be able to identify and establish additional relationships with such sources, if necessary, in a timely manner or at all, and what the terms and costs of such new arrangements would be, or that such suppliers would be able to supply our potential commercial needs. Furthermore, in the event our primary manufacturer cannot meet our needs, any switch to an alternative manufacturer, if available, would result in a significant delay, would require FDA approval, and cause material additional costs.

As further described in these risk factors, the manufacturers of biologic products must comply with strictly enforced cGMP requirements, state and federal regulations, as well as foreign requirements when applicable. Any failure by us or our contract manufacturing organizations to adhere to or document compliance to such regulatory requirements could lead to a delay or interruption in the availability of our program materials for clinical trials or commercial use, among other consequences. If we or our manufacturers fail to comply with the FDA, EMA, or other regulatory authorities, it could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, clinical holds or termination of clinical trials, warning or untitled letters, regulatory communications warning the public about safety issues with a product, import or export refusals, license revocation, seizures, detentions, or recalls of product candidates or product, operating restrictions, criminal prosecutions or debarment, suits under the civil False Claims Act, corporate integrity agreements, or consent decrees any of which could significantly and adversely affect supplies of our product candidates and our business, financial conditions and results of operations could be materially adversely affected.

Our current dependence upon others for the manufacture of our product candidates may also adversely affect our business, results of operations, financial condition, and our ability to commercialize any product candidates that receive regulatory approval on a timely and competitive basis.

Fast Track designation by the FDA or any future designations may not lead to a faster development, regulatory review or approval process and it does not increase the likelihood that any of our product candidates will receive marketing approval.

We have received Fast Track therapy designation for CTI-1601 for the treatment of Friedreich's ataxia. We may, in the future, apply for other accelerated programs from the FDA (such as breakthrough therapy or accelerated approval) for CTI-1601 or future product candidates. Designation for these programs is within the discretion of the FDA. Accordingly, even if we believe CTI-1601 or a future product candidate meets the criteria for designation, the FDA may disagree. In any event, the receipt of a designation may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and, in any event, does not assure ultimate approval by the FDA. In addition, even though CTI-1601 has been designated as Fast Track, the FDA may later decide that it no longer meets the criteria for designation and revoke it. If we apply for designation to additional accelerated programs from the FDA for CTI-1601 or future product candidates, the FDA might not grant the designation. If we apply for any similar programs in foreign countries for CTI-1601 or future product candidates, those designations also might not be granted by the regulatory authorities of those countries. Any of the above could adversely affect our business, financial condition and results of operations.

If we fail to maintain orphan drug designation or other regulatory exclusivity for CTI-1601 or obtain such exclusivity for any of our other product candidates in the future, our competitive position would be harmed.

We received orphan drug designation from the FDA for CTI-1601 in July 2017. In the United States, orphan drug designation entitles a party to financial incentives such as tax advantages and user-fee waivers. In addition, if a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug for the same indication for seven years, except in limited circumstances, including if the FDA concludes that the later drug is clinically superior to the approved drug. A drug is clinically superior if it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We may lose orphan drug exclusivity if we are unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Moreover, orphan drug exclusivity may not effectively protect our product candidates from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care.

We have also received orphan drug designation for CTI-1601 in the EU. In the EU, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug. In the EU, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable so that market exclusivity is no longer justified. Loss of orphan drug designation for CTI-1601 or the failure to obtain such designation in other countries or for any future product candidates could adversely affect our business, financial condition and results of operation.

Although we have obtained rare pediatric disease designation for CTI-1601, we may not be eligible to receive a priority review voucher in the event the FDA determines we no longer meet the criteria for designation, revokes the designation or that FDA approval does not occur prior to September 30, 2026.

We received rare pediatric disease designation from the FDA for CTI-1601 in 2019. We may, in the future, apply for rare pediatric disease designation from the FDA for future product candidates that may qualify for designation. Vouchers for rare pediatric disease drugs are awarded when the designated drug receives approval. CTI-1601 may not receive approval and therefore, we may not receive a voucher. In addition, even though CTI-1601 has been designated as a drug for a rare pediatric disease, the FDA may later decide that it no longer meets the criteria for designation, revoke the designation or not award the voucher. If we apply for designation for future product candidates as drugs for rare pediatric diseases, the FDA may not grant the designation. The failure to maintain rare pediatric disease designation for CTI-1601 or if FDA approval does not occur prior to September 30, 2026 could result in the inability to receive a priority review voucher which could adversely affect our business, financial condition and results of operations.

Changes in regulatory requirements, FDA guidance, guidance from other regulatory authorities or unanticipated events during our clinical trials of CTI-1601 may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or guidance from EMA or unanticipated events during our clinical trials may force us to terminate or adjust our clinical program. The FDA, or the applicable regulatory authorities may impose additional clinical trial and/or nonclinical study requirements. Amendments to our clinical trial protocols would require resubmission to the FDA, or the applicable regulatory authorities as well as IRBs and ethics committees for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, or nonclinical studies and/or post-market studies, the commercial prospects for CTI-1601 or any other potential product candidates may be harmed and our ability to generate product revenue will be delayed, and it would materially adversely affect our business, financial condition and results of operations.

In order to market any product outside of the United States, we must comply with numerous and varying regulatory requirements of other countries regarding drug development and commercialization. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. In addition, on January 31, 2020, the United Kingdom exited from the European Union, or Brexit. A transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. Over the past year, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) has issued numerous guidances to address how drugs and devices are to be regulated in the UK post-Brexit. However, the ultimate impact of the "leave" is not clear as there is still some legal and practical uncertainty surrounding the regulation of drugs in the UK and how such regulation may diverge with regulation in the EU.

Regulatory requirements governing biologic products have changed frequently and may continue to change in the future. Such requirements may lengthen the regulatory review process, require us to perform additional nonclinical studies or clinical trials, and increase our costs, or may force us to delay, limit or terminate certain of ours programs.

Regulatory requirements governing biologic drug products are still evolving and may continue to change in the future. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for CTI-1601 for the treatment of Friedreich's ataxia or any other future protein replacement therapy product candidates in any indication, if at all. Regulatory review agencies 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 our product candidates or lead to significant post-approval studies, limitations or restrictions. Delays, failure or unexpected costs in obtaining, the regulatory approval necessary to bring our product candidates to market could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, the clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. 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 product candidates.

The clinical trials of CTI-1601 and any future product candidates are, and the manufacturing and marketing of CTI-1601 and any future product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries, such as within the EU, where we intend to seek regulatory approval of, and market, any product candidate.

Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through nonclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years. If marketing approval is obtained, it will likely include post-marketing studies, and other post-marketing requirements, and surveillance such as Risk Evaluation and Mitigation Strategies, or REMS, which will require the expenditure of substantial resources beyond the proceeds we currently have on hand.

Furthermore, we are not permitted to market CTI-1601 in the United States or the EU until we receive approval of a BLA from the FDA or a MAA from the EMA, or in any other foreign countries until we receive the requisite marketing approval from such countries. The development of drugs for Friedreich's ataxia or other rare diseases may require initial nonclinical studies, early and usually smaller, clinical trials and randomized, double-blind placebo controlled long-term safety and efficacy trials in order to test the safety and efficacy of the drug.

CTI-1601 is currently in Phase 1 clinical trials in the United States and will require substantial further clinical development before we can submit a BLA to the FDA. Development and/or regulatory programs for CTI-1601 in any countries other than the United States (such as a MAA to the EMA) is only in very preliminary stages and may require substantial further development in those countries prior to regulatory submissions seeking regulatory approval for marketing.

Even after successful completion of clinical trials, there is a risk that the FDA or other regulatory agencies may request further information from us, disagree with our findings or otherwise undertake a lengthy review of our submission.

The FDA and certain European regulatory authorities may delay, limit or deny testing or approval of CTI-1601 for many reasons, including, among others:

- we may not be able to demonstrate that CTI-1601 is safe and effective to the satisfaction of the FDA or the EMA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or the EMA for marketing approval;
- the FDA or the EMA may disagree with the number, design, size, duration, conduct or implementation of our clinical trials;
- the FDA or the EMA may require that we conduct additional nonclinical studies or clinical trials;
- the FDA or the EMA may not approve the formulation, manufacturing, labeling or specifications of CTI-1601;
- the contract research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA or the EMA may find the data from nonclinical studies and clinical trials insufficient to demonstrate that CTI-1601's clinical and other benefits outweigh its safety risks;
- the FDA or the EMA may disagree with our interpretation of data from our nonclinical studies or clinical trials;
- the FDA or the EMA may not accept data generated at our clinical trial sites;

- if and when our BLA is submitted, the FDA could require an FDA advisory committee assessment, or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional nonclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the FDA could require development of a REMS as a condition of approval or post-approval, or may not agree with our proposed REMS, or may impose additional requirements, including requirements that limit the promotion, advertising, distribution, or sales of CTI-1601;

- the FDA or the EMA may find deficiencies with or not approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or

- the FDA or the EMA may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain and/or maintain regulatory approval for and successfully market CTI-1601. Any delay or failure in obtaining required approvals could have a material adverse effect on our business, financial condition and results of operations. This process can take many years and will likely require the expenditure of substantial resources. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and be commercialized. It is possible that the FDA or other regulatory agencies will not approve any application that we submit. It is possible that our product candidates may not obtain appropriate regulatory approvals necessary for us to commence clinical trials for our product candidates. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure that CTI-1601, or any other of our potential product candidates will be successfully developed or commercialized.

We are subject to healthcare laws and regulations, and health information privacy and security laws, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of CTI-1601 or any potential product candidates, if approved. Our future arrangements with third-party payors will expose us broadly to applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute CTI-1601 or potential product candidates, if we obtain marketing approval. In addition, we may be subject to patient privacy regulation by both the federal government and the states or other countries in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

- the federal false claims laws impose criminal and civil penalties, including those from civil whistleblower or qui tam actions pursuant to the federal False Claims Act, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

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

- the federal transparency requirements, sometimes referred to as the "Sunshine Act," under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or ACA, require manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations and would materially adversely affect our business, financial condition and results of operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Healthcare legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates.

The commercial potential for our approved products, if any, could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry. New laws, regulations or judicial decisions or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could adversely affect our business, operations and financial condition. The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that may affect our ability to profitably sell our product and product candidates, if approved. The United States government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

The Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. There have been significant ongoing administrative, executive and legislative efforts to modify or eliminate the Affordable Care Act. For example, the Tax Act enacted on December 22, 2017, repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code, commonly referred to as the individual mandate. The Trump administration issued

executive orders which sought to reduce burdens associated with the Affordable Care Act and modified how it was implemented. Other legislative changes have been proposed and adopted since the passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than $1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken, However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The Affordable Care Act has also been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court which heard oral arguments in the case on November 10, 2020. A ruling is expected in 2021. Further changes to and under the Affordable Care Act remain possible, although the new Biden administration has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. President Biden indicated that he intends to use executive orders to undo changes to the Affordable Care Act made by the Trump administration and would advocate for legislation to build on the Affordable Care Act. It is unknown what form any such changes or any law proposed to replace the Affordable Care Act would take, and how or whether it may affect our business in the future. We expect that changes to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain and maintain profitability of our product and product candidates, if approved.

Even if approved, reimbursement policies could limit our ability to sell product candidates that we elect to sell on our own.

If approved by regulatory authorities, market acceptance and sales of product candidates that we elect to sell on our own will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for CTI-1601 or future product candidates that we elect to sell on our own and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, product candidates that we elect to. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize product candidates that we elect to sell.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of product candidates that we elect to sell on our own with other available therapies. If reimbursement for product candidates that we elect to sell on our own is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our business, financial conditions and results of operations could be materially adversely affected.

Even if we obtain regulatory and marketing approval for a product candidate, our product candidates will remain subject to regulatory oversight.

Even if we receive marketing and regulatory approval for CTI-1601 or a future product candidate, regulatory authorities may still impose significant restrictions on the indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. CTI-1601 or future product candidates will also be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug. Any regulatory approvals that we receive for CTI-1601 may also be subject to a REMS, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-approval clinical trials, and surveillance to monitor the quality, safety and efficacy of the product, all of which could lead to lower sales volume and revenue. For example, the holder of an approved BLA or NDA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA or NDA. The holder of an approved BLA or NDA also must 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 cGMP requirements and adherence to commitments made in the BLA or NDA or foreign marketing application. If we, or a regulatory authority, discover(s) previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we or our contractors fail to comply with applicable regulatory requirements following approval of CTI-1601, a regulatory authority may:

- issue a warning letter asserting that we are in violation of the law;
- request voluntary product recalls;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or NDA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise require the withdrawal of the product from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

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 CTI-1601 and adversely affect our business, financial condition, results of operations and prospects.

In addition, the FDA's policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of CTI-1601. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially and adversely affect our business, financial condition, results of operations and prospects.

Even if we receive marketing approval for CTI-1601 in the United States, we may never receive regulatory approval to market CTI-1601 outside of the United States.

We may pursue marketing approval for CTI-1601 in the United States, the European Union and in other jurisdictions worldwide. In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other jurisdictions, including potential additional clinical trials and/or nonclinical studies. Approval procedures vary among jurisdictions and can involve additional testing and additional administrative review periods. The time required to obtain approvals in other jurisdictions might differ from that required to obtain FDA approval. The marketing approval processes in other jurisdictions may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one jurisdiction does not necessarily ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process or commercial activities in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market a product candidate in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, financial condition, results of operations and prospects.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

The prevalence of FA is estimated to be four times greater in the European Union than in the United States, and, therefore, represents our largest potential market for CTI-1601Our future profitability will depend, in part, on our ability to commercialize CTI-1601 and future product candidates in the European Union and other foreign markets for which we may rely on collaborations with third parties. If we commercialize a product candidate in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for a product candidate in foreign markets;
- compliance with the Foreign Corrupt Practices Act of 1977, or FCPA;
- our inability to directly control commercial activities because we may need to rely on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;

- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Sales in the EU and other foreign markets of a product candidate could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell CTI-1601, we may not be able to generate any revenue.

We do not currently have an established infrastructure for the sales, marketing and distribution of biologic or drug products in the United States or foreign countries. In order to market a product candidate, if approved by the FDA or any other regulatory authority, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even if we receive marketing approval for CTI-1601, we may not achieve broad market acceptance, which would limit the revenue that we generate from our sales.

The commercial success of CTI-1601, if developed and approved for marketing by the FDA or EMA or other applicable regulatory authorities, will depend upon the market size for, and the awareness and acceptance of CTI-1601 among the medical community, including physicians, patients, advocacy groups and healthcare payors. Market acceptance of CTI-1601, if approved, will depend on a number of factors, including, among others:

- If the actual number of patients with Friedreich's ataxia is lower than we believe;
- the relative convenience and ease of subcutaneous injections as the necessary method of administration;
- the prevalence and severity of any adverse side effects associated with CTI-1601;
- limitations or warnings contained in the labeling approved for CTI-1601 by the FDA, EMA, or other regulatory authorities, such as a "black box" warning or if any approval that we obtain is based on a narrower definition of possible patient populations;
- availability of alternative treatments, including any competitive Friedreich's ataxia therapies in development that could be approved or commercially launched prior to approval of CTI-1601;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;

- pricing;
- patient acceptance of the cost and inconvenience associated with refrigerated storage for CTI-1601;
- payor acceptance;
- increased political pressure on pharmaceutical pricing;
- increased pressure on orphan drug pricing for affected patient groups;
- the impact of any future changes in U.S. healthcare, including medical financial assistance or a transition to a single-payer system;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of CTI-1601 through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness or ability of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that the FDA may require development of a REMS, as a condition of approval or post-approval or may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution or sales of our product candidates.

If CTI-1601 is approved but does not achieve an adequate level of acceptance by patients, advocacy groups, physicians and payors, we may not generate sufficient revenue from CTI-1601 to become or remain profitable and our business, financial condition and results of operations could be materially adversely affected. Our efforts to educate the medical community and third-party payors about the benefits of CTI-1601 may require significant resources and may never be successful.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as CTI-1601 or any potential product candidates, if approved. If we receive marketing approval for CTI-1601, or any potential product candidates, physicians may prescribe our product candidates to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion and required that they enter into corporate integrity agreements with the Office of Inspector General of the Department of Health and Human Services. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of CTI-1601 or any potential product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business, financial condition and results of operations.

Competing technologies could emerge, adversely affecting our opportunity to generate revenue from the sale of CTI-1601.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including biosimilar and gene therapy competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to CTI-1601 or any other potential product candidates. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and results of operations will be adversely affected.

We may face competition from biosimilars and may face increasing competition over time.

We may face competition from biosimilars in both the United States and Europe, and over time we may face increasing biosimilar competition. To the extent that governments adopt more permissive approval frameworks and competitors are able to obtain broader or expedited marketing approval for biosimilars, the rate of increased competition for our biologic drug products could accelerate. Expiration or successful challenge of applicable patent rights could trigger such competition, and we could face more litigation regarding the validity and/or scope of our patents. Our products may also experience greater competition from lower cost biosimilars or generics that come to market when branded products that compete with our products lose their own patent protection.

In the EU, the European Commission has granted marketing authorizations for biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued in 2005. In addition, in an effort to spur biosimilar utilization and/or increase potential healthcare savings, some EU countries have adopted biosimilar uptake measures such as requiring physician prescribing quotas or promoting switching or pharmacy substitution of biosimilars for the corresponding reference products, and other countries may adopt similar measures. Some EU countries may impose automatic price reductions upon market entry of the second or third biosimilar competitor.

In the United States, the ACA authorized the FDA to approve biosimilars via a separate, abbreviated pathway. A growing number of companies have announced that they are in varying stages of development of biosimilar versions of existing biotechnology products. Some companies pursuing development of biosimilars may challenge our patents well in advance of the expiration of our material patents. The U.S. pathway includes the option for biosimilar products meeting certain criteria to be approved as interchangeable with their reference products. Some companies developing biosimilars may seek to register their products as interchangeable biologics, which could make it easier for prescribers or pharmacists to substitute those biosimilars for our products. In addition, critics of the 12-year exclusivity period in the biosimilar pathway law will likely continue to seek to shorten the data exclusivity period and/or to encourage the FDA to interpret narrowly the law's provisions regarding which new products receive data exclusivity. While we are unable to predict the precise impact of biosimilars, we expect in the future for there to be greater competition in the United States as a result of biosimilars and downward pressure on product prices and sales. This additional competition could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Business

If we are unable to manage expected growth in the scale and complexity of our operations, including attracting and hiring additional qualified management, our performance may suffer.

We are an early-stage clinical biotechnology company with a small number of employees, and our management systems currently in place are not likely to be adequate to support our future growth plans. As a result, we are highly dependent on our management and scientific personnel. The loss of the services of any of our executive officers, other key employees or consultants and other scientific advisors in the foreseeable future, might impede the achievement of our research, development and commercialization objectives. We rely on consultants and advisors, including scientific, nonclinical, manufacturing and clinical advisors, to assist us in formulating our development and commercialization strategy. These consultants and advisors may be employed by other employers and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the competition for talent, particularly with the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products.

Recruiting and retaining qualified scientific, medical clinical, manufacturing, quality assurance, regulatory, legal, public company financial, business, sales, marketing and commercial personnel and implementing and improving our operational, financial and management systems will be critical to our ability to grow and succeed. These demands also will require the hiring of additional executive or management-level personnel or the development of additional expertise by our senior management personnel. Hiring a significant number of additional employees, particularly those at the executive or management level, would increase our expenses significantly. In addition, we may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Moreover, delays or failures in clinical trials may also make it more challenging to recruit and retain qualified scientific personnel. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our business strategy will be limited and our business, financial condition and results of operations would be adversely affected.

Further, if we fail to expand and enhance our operational, financial and management systems in conjunction with potential future growth, such failure could have a material adverse effect on our business, financial condition and results of operations. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development, business and growth goals.

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

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed 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 results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

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

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions or alliances.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate such businesses with our existing operations and company culture.

We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delays or prevents us from realizing their expected benefits or enhancing our business. We cannot be certain that, following any such transaction, we will achieve the expected synergies to justify the transaction and it could adversely affect our business, financial condition and results of operations.

We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans or expand our internal efforts and growth.

Our development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For CTI-1601, and any future product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates in some or all markets.
We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration for CTI-1601 or other potential product candidates will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the applicable product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. The terms of any collaboration or other arrangement that we may establish may not be favorable to us.

We may also be restricted under existing license agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable or unwilling to do so, we may have to curtail the development potential product candidates for which we are seeking to collaborate, reduce or delay our development program or one or more of our other development programs, delay potential commercialization in some or all markets or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense, including potentially increasing our infrastructure and investment outside the United States. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. In addition, such efforts may require diversion of a disproportionate amount of our attention away from other day-to-day activities and require devotion of a substantial amount of our time to managing these activities.

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration could adversely affect our business, financial condition, results of operations and could harm our business reputation.

We face risks related to health epidemics, including the ongoing COVID-19 pandemic, and other outbreaks of communicable diseases, which could significantly disrupt our operations and may materially and adversely affect our business and financial conditions.

Our business could be adversely impacted by the effects of the coronavirus or other epidemics. In December 2019, a novel strain of the coronavirus, or COVID-19, emerged in China and the virus has now spread to almost every country, including the United States. In an effort to halt the outbreak of COVID-19, governments of countries around the world have placed significant travel restrictions or advisories on travel within their respective borders and have instituted shelter-in-place policies that have led to extended business closures. The extent to which the coronavirus and global efforts to contain its spread will impact our operations will depend on future developments, which are highly uncertain and cannot be predicted at this time, and include the duration, severity and scope of the outbreak and the actions taken to contain or treat the coronavirus outbreak. The continued spread of the coronavirus globally could materially and adversely impact our operations, including without limitation, our manufacturing and supply chain for CTI-1601 and ongoing and planned clinical trials, which have faced, and could continue to face, enrollment difficulties as hospitals or clinical trials sites experience closures. The pandemic resulted in the temporary stoppage of our Phase 1 clinical trials studying CTI-1601 in patients with Friedreich's ataxia after the completion of two cohorts. In July 2020, we resumed our Phase 1 clinical trials of CTI-1601.We are conducting the clinical trials at one clinical trial site in New Jersey. Because Friedreich's ataxia is a rare disease, there are a limited number of patients in close proximity to the clinical trial site and clinical trial patients travel from throughout the United States to the clinical trial site to participate. The travel advisories and risk of infection related to COVID-19 have presented increased risks to patients traveling to our clinical trial site for dosing. While top line results from the Phase 1 clinical trials were originally expected by the end of 2020, the delay in the clinical trial timeline caused by the ongoing impact of COVID-19 has resulted in top line results being delayed until the second quarter of 2021. In addition, employee health and availability could be impacted, which may have a material and adverse effect on our business, financial condition and results of operations. A significant outbreak of coronavirus could also result in widespread global health crisis that could adversely affect global economies and financial markets resulting in an economic downturn that could have a material adverse effect on our business and prospects.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we may operate has established its own data security and privacy frameworks with which we must comply. For example, the European Union's General Data Protection Regulation 2016/679, or GDPR, imposes strict obligations on the processing of personal data, including personal health data, and the free movement of such data. The GDPR applies to any company established in the European Union as well as any company outside the European Union that processes personal data in connection with the offering of goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, obligations relating to: processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; implementing safeguards to protect the security and confidentiality of personal data; and transferring personal data to countries outside the European Union, including the United States. The GDPR imposes additional obligations and risks upon our business and substantially increases the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million or 4% of total worldwide annual revenue, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages. Given the breadth and depth of changes in data protection obligations, if we are required to comply with the GDPR's requirements, we will be required to spend significant time and resources to review our technologies, systems and practices, as well as those of any third-party service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices or lead to government enforcement actions, private litigation or significant fines and penalties against us, reputational harm and could have a material adverse effect on our business, financial condition or results of operations.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The use of CTI-1601 and other potential product candidates in clinical trials, if any, and the sale of CTI-1601 and other potential product candidates, if developed and approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with CTI-1601 or other potential product candidates. For example, we may be sued if any product we develop allegedly causes injury or death or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under consumer protection acts in other jurisdictions. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for CTI-1601 or our other potential product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- voluntary product recalls, withdrawals, or labeling restrictions;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully commercialize CTI-1601 or other potential product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a $5 million aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If we obtain marketing approval for CTI-1601 or other potential product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business, results of operations and prospects could be materially adversely affected.

Risks Related to Our Reliance on Third Parties

We have limited experience in conducting or supervising clinical trials and must outsource all clinical trials. As a result, many important aspects of our drug development programs are outside of our direct control.

We have limited experience in conducting or supervising clinical trials that must be performed to obtain data to submit in concert with applications for approval by the FDA, the EMA or other comparable foreign regulatory authorities. As a result, we expect to continue to rely on CROs, clinical data management organizations and consultants to design, conduct, supervise and monitor our nonclinical studies and clinical trials. We and our CROs are required to comply with various regulations, including the FDA's regulations commonly referred to as good clinical practices, or GCPs, which are enforced by regulatory agencies, including the FDA, and comparable foreign regulatory authorities to ensure the health, safety and rights of patients are protected in clinical development and clinical trials, and that trial data integrity is assured. Regulatory authorities ensure compliance with these requirements through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Our expected reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. If we or any of our CROs fail to comply with applicable requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with such requirements. In addition, our clinical trials must be conducted with products produced under cGMP requirements, which mandate, among other things, the methods, facilities and controls used in manufacturing, processing and packaging of a drug product to ensure its safety and identity. Failure to comply with these regulations may require us to repeat nonclinical studies and/or clinical trials, which would delay the regulatory approval process, and could also subject us to enforcement action, up to and including, civil and criminal penalties, which would materially adversely affect our business, financial condition and results of operations.

Our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and preclinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed or reduced. In addition, operations of our CROs could be affected by earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions. If their facilities are unable to operate because of an accident or incident, even for a short period of time, some or all of our research and development programs may be harmed or delayed, and our operations and financial condition could suffer.

We have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. We currently have a small number of employees, which limits the internal resources we have available to engage new third-party providers, if necessary, and monitor existing third-party providers. To the extent we are unable to engage new third-party providers, if necessary, and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, results of operation and prospects.

We rely on third-party supply and manufacturing partners for drug supplies for our research and development, nonclinical activities, and clinical activities, and may do the same for any commercial supplies of our product candidates.

We rely on third-party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, nonclinical and clinical study drug substance and product. We have not yet manufactured or formulated any product candidate on a commercial scale and may not be able to do so for any of our product candidates. We will work to develop and optimize our manufacturing process; however, we cannot be sure that the process will result in therapies that are safe, potent or effective.

We do not own manufacturing facilities or supply sources for such components, nonclinical and clinical study drug substance, product and materials, including devices that may be required for administration, but may develop these capabilities in the future. There can be no assurance that our supply of research and development, nonclinical and clinical development of drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or will be of satisfactory quality or continue to be available at acceptable prices. In particular, replacement of any product formulation manufacturer we may engage could require significant effort and expertise because there may be a limited number of qualified replacements.

In the event that any of our suppliers or manufacturers fails to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We also rely on third parties to store master and working cell banks. We currently have one master cell bank and one working cell bank for CTI-1601 and believe we would have adequate backup should any cell bank be lost in a catastrophic event. However, it is possible that we could lose multiple cell banks and have our manufacturing severely impacted by the need to replace the cell banks, which could materially and adversely affect our business, financial condition and results of operations.

We may rely on third party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business, financial condition and results of operations in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;

- subjecting our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

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

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for CTI-1601, are subject to extensive regulation. Some components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA or NDA on a timely basis and where required, must adhere to the FDA's or other regulator's good laboratory practices, or GLPs, and cGMP regulations enforced by the FDA or other regulator through facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of CTI-1601 or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of CTI-1601 or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA or other regulatory approval of the products will not be granted.

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

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

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. The number of manufacturers with the necessary manufacturing capabilities is limited. In addition, an alternative manufacturer would need to be qualified through a BLA or NDA supplement or similar regulatory submission which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

These factors could also cause the delay of manufacturing development, clinical trials, regulatory submissions, required approvals or commercialization of CTI-1601 or any other product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed, or we could lose potential revenues. Any of the above would materially adversely affect our business, financial condition and results of operations.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could materially increase our costs and potential liability.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sublicensees' exercise of rights under the agreement. With respect to our collaboration and contract service agreements, we indemnify our collaborators from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consulting agreements, we indemnify consultants from claims arising from the good faith performance of their consulting services.

Should our obligation under an indemnification provision exceed applicable insurance coverage or should we be denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we may be exposed to risks related to those collaborations and alliances.

Biotechnology companies sometimes become dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of product candidates. If we elect to enter into collaborative arrangements or strategic alliances, these arrangements may place the development of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us, which could adversely affect our business, financial condition and results of operations.

Dependence on collaborative arrangements or strategic alliances would subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the relevant product candidates;
- our collaborators may experience financial difficulties;
- we may be required to relinquish important rights, such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and
- collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology or maintain issued patents which are sufficient to protect CTI-1601 or potential product candidates, third parties could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

With respect to our patent portfolio, we in-license from WFUHS certain issued U.S. patents that relate to CTI-1601 and its use for treating Friedreich's ataxia. We also in-license from IU a pending international and a United States non-provisional application that relates to the composition of CTI-1601 and methods of use, and certain U.S. patents relating to materials and methods of use relating to the development of CTI-1601. We also own or co-own pending international and United States non-provisional applications and United States provisional applications relating to methods of use of CTI-1601, biomarkers and to our platform technology.

In some cases, we have only filed provisional patent applications on certain aspects of our technologies and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications.

With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

We cannot provide any assurances that any of our pending patent applications that mature into issued patents will include claims with a scope sufficient to protect CTI-1601, or other potential product candidates. Other parties have developed technologies that may be related or competitive to our approach and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, ex parte reexamination, or inter partes review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize CTI-1601, and other potential product candidates.

Furthermore, though an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our potential future sales.

Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering CTI-1601 are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered CTI-1601, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect CTI-1601 or any other products or product candidates;
- any of our pending patent applications will issue as patents;
- we will be able to successfully develop and, if approved, commercialize CTI-1601 before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents of others.

We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us and have non-compete agreements with some, but not all, of our consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors. If we are unable to adequately protect our proprietary technology or maintain issued patents which are sufficient to protect CTI-1601 or potential future product candidates, third parties could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Certain of the patents we license relating to CTI-1601 will expire by 2025 and we will lose our ability to rely upon these patents to prevent competing products, which may impair our ability to generate revenue.

We have in-licensed certain patents relating to CTI-1601 from WFUHS. The U.S. patents relating to CTI-1601 and its use for the treatment of Friedreich's ataxia expire in 2024 and 2025, respectively. When these patents expire, we will be unable to use these patents to try to block others from marketing CTI-1601 in the United States We have also in-licensed an international and a United States non-provisional patent application relating to the composition of CTI-1601 and methods of use from IU, which, if issued as a patent, would expire at the earliest in 2040. We cannot predict whether these patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties. When these various patents, if issued, expire, we will be unable to use the patents to try to block others from marketing CTI-1601 in the United States.

We own certain United States provisional applications and United States and international non-provisional applications relating to our platform technology which, if issued as patents, would be expected to expire in 2040-2041. The provisional applications may not be timely converted into non-provisional applications, and we cannot predict whether these provisional applications and non-provisional patent applications will issue as patents in any particular jurisdiction, or whether the claims of any issued patents will provide sufficient protection from competitors or third parties for potential product candidates. When these various patents expire, we will be unable to use the patents to try to block others from marketing products pertaining to our platform technology.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product 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.

Once our patents expire, we will be subject to competition from third parties who will be able to use the intellectual property covered by these patents, which could impair our ability to generate revenue and could adversely affect our business, financial condition and results of operations.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing CTI-1601 or other potential product candidates, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot ensure that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Third parties may allege that CTI-1601 or our other potential product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license.

In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing CTI-1601.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing CTI-1601;
- cease preparations or development of our other potential product candidates;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign or rename the trademarks or trade names of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business, financial condition and results of operations. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

We have systems in place to remind us to pay periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees, and we employ an outside law firm to pay these fees. The U.S. Patent and Trademark Office and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ an outside law firm and other professionals to help us comply, and 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. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs, our competitors may be able to enter the market, which would have a material adverse effect on our business.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe on our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of our or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing which could materially adversely affect our business, financial condition and results of operations.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business, financial condition and results of operations could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States, which could adversely affect our business, financial condition and results of operations.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering our product candidate, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also 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 and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot ensure that there is no invalidating prior act, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business, financial condition, and results of operations.

We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from 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 and other intellectual property protection, particularly those relating to biopharmaceuticals, 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 2020 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, could put 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, which would materially adversely affect our business, financial condition and results of operations.

We are dependent on licensed intellectual property for CTI-1601. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing CTI-1601, if approved.

We have an exclusive license with WFUHS, pursuant to which we exclusively license certain patent rights relating to the TAT-frataxin fusion protein and its use, on a worldwide basis. We have an exclusive license with IU, pursuant to which we exclusively license certain patent rights relating to CTI-1601 and its use for the treatment of mitochondrial diseases, on a worldwide basis.

Our license agreements with WFUHS and IU impose, and we expect our future license agreements will impose, various development, diligence, commercialization, and other obligations on us in order to maintain the licenses. In spite of our efforts, WFUHS, IU, or a future licensor might conclude that we have materially breached our obligations under such license agreements and seek to terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these licenses are terminated, or if the underlying patent rights licensed thereunder fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates or of CTI-1601. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

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

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize CTI-1601, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

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

Our in-licensed patent rights from WFUHS and IU were funded in part by the U.S. government and are therefore subject to certain federal regulations. 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 license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or 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 in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

We have not yet registered trademarks for a commercial trade name for CTI-1601 or other potential product candidates and failure to secure such registrations could adversely affect our business, financial condition and results of operations.

We have not yet registered trademarks for a commercial trade name for CTI-1601 or other potential product candidates. Any future trademark applications may be rejected during trademark registration proceedings. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, the U.S. PTO and comparable agencies in many foreign jurisdictions give third parties an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Any trademarks we have obtained or may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our products that are approved for marketing from the products of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for CTI-1601, our business may be materially harmed.

Depending upon the timing, duration and specifics of development and FDA marketing approval of CTI-1601 or our other potential product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain a patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues, business, financial condition and results of operations could be materially adversely affected.

Our proprietary rights may not adequately protect our technologies, which may adversely affect our position in the market, business, financial condition and results of operations.

We rely on unpatented trade secrets, know-how, and technology, which are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval process. We seek to protect trade secrets, in part, by entering into confidentiality agreements with employees, consultants and others. These parties may breach or terminate these agreements or may refuse to enter into such agreements with us, and we may not have adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection for our trade secrets or other proprietary information or result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential information or other breaches of the agreements. Despite our efforts to protect our trade secrets, we or our board members, employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors.

If we fail to maintain trade secret protection, our competitive position may be adversely affected. Competitors may also independently discover our trade secrets. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secrets against them and our business, financial condition and results of operations could be harmed.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. The Leahy Smith America Invents Act, or the Leahy Smith Act, enacted in September 2011, brought significant changes to the U.S. patent law system. These include provisions that affect the way patent applications are prosecuted and may affect patent litigation. The United States Patent Office continues to develop and implement new regulations and procedures to govern administration of the Leahy Smith Act, and many of the substantive changes to patent law associated with the Leahy Smith Act became effective on March 16, 2013. The Leahy Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations, financial condition and prospects.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the U.S. PTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our employees' former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we are not aware of any claims currently pending against us, we may be subject to claims that we or our employees inadvertently or otherwise used or disclosed the trade secrets or other proprietary information of our employees' former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to develop and commercialize CTI-1601 or our other potential product candidates, which would materially adversely affect our business, financial condition and results of operations.

Risks Related to Our Common Stock

Our stock price could be highly volatile, and purchasers of our common stock could incur substantial losses.

The market price of our common stock could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology, and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- Our ability to obtain regulatory approvals for product candidates, and delays or failures to obtain such approvals;
- the results of current, and any future, nonclinical or clinical trials of CTI-1601 or any of our future product candidates;
- the entry into, or termination of, key agreements, including key licensing or collaboration agreements;
- the failure of CTI-1601 or any of our future product candidates, if approved for marketing and commercialization, to achieve commercial success;
- issues in manufacturing our approved products, if any, or product candidates;
- the initiation of material developments in, or conclusion of, disputes or litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- announcements by commercial partners or competitors of new commercial products, clinical progress (or the lack thereof), significant contracts, commercial relationships, or capital commitments;
- adverse publicity relating to our markets, including with respect to other products and potential products in such markets;
- the introduction of technological innovations or new therapies competing with our potential products;
- the loss of key employees;

- general and industry-specific economic conditions potentially affecting our research and development expenditures;
- changes in the structure of health care payment systems;
- adverse regulatory decisions;
- trading volume of our common stock; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies or the biotechnology sector. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management's attention and resources, which could significantly impact our profitability and reputation.

We must maintain effective internal controls over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a public company, the Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our disclosure controls and procedures quarterly and the effectiveness of our internal control over financial reporting at the end of each fiscal year.

The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit committee be advised and regularly updated on management's review of internal control over financial reporting.

Our management may not be able to effectively and timely implement controls and procedures that adequately remediate our material weaknesses and respond to the increased regulatory compliance and reporting requirements that are applicable to us as a public company. If we fail to staff our accounting, finance and information technology functions adequately or maintain internal control over financial reporting adequate to meet the demands that are placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act, or to otherwise remediate our existing or any future material weaknesses in internal control over financial reporting, or identify any additional material weaknesses, our business and reputation may be harmed and our stock price may decline. Furthermore, investor perceptions of us may be adversely affected, which could cause a decline in the market price of our common stock.

Ownership of our common stock is highly concentrated, and it may prevent other stockholders from influencing significant corporate decisions.

Entities affiliated with Deerfield Management Company beneficially own or control approximately 32.2% of our outstanding common stock (assuming full exercise of our outstanding pre-funded warrants and no exercise of outstanding options) as of December 31, 2020, on a fully-diluted basis. Accordingly, such entities have substantial influence over the outcome of a corporate action by us requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. These stockholders also may exert influence in delaying or preventing a change in control of the combined company, even if such change in control would benefit our other stockholders.

We are a smaller reporting company. We cannot be certain whether the reduced disclosure requirements applicable to smaller reporting companies will make our common shares less attractive to investors or otherwise limit our ability to raise additional funds.

We are currently a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act, and have elected to take advantage of certain of the scaled disclosures available to smaller reporting companies, including simplified executive compensation disclosures in our filings, exemption from the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that an independent registered accounting firm provide an attestation report on the effectiveness of internal control over financial reporting and certain other decreased disclosure obligations in our SEC filings, including, among other things, only being required to provide two years of audited financial statements in annual reports. Reduced disclosure in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.

Provisions in our certificate of incorporation and bylaws may delay or prevent an acquisition or a change in management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of the board of directors to issue preferred stock without stockholder approval. In addition, because we are in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporations Law, or DGCL, which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors, which is responsible for appointing the members of management.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain our future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be stockholders' sole source of gain, if any, for the foreseeable future.

General Risk Factors

Our failure to meet the continued listing requirements of The Nasdaq Stock Market LLC could result in a delisting of our Common Stock.

If we fail to satisfy the continued listing requirements of The Nasdaq Stock Market LLC, or Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase shares of common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow the common stock to become listed again, stabilize the market price or improve the liquidity of the common stock, prevent the common stock from dropping below the Nasdaq minimum bid price requirement or prevent future noncompliance with Nasdaq's listing requirements.

Financial reporting obligations of being a public company in the United States are expensive and time-consuming, and our management will be required to devote substantial time to new compliance matters.

The obligations of being a public company in the United States requires significant expenditures and will place significant demands on our management and other personnel, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended, and the rules and regulations regarding corporate governance practices, including those under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, and the listing requirements of Nasdaq on which our securities are listed. These rules require the establishment and maintenance of effective disclosure and financial controls and procedures, internal control over financial reporting and changes in corporate governance practices, among many other complex rules that are often difficult to implement, monitor and maintain compliance with. Moreover, despite recent reforms made possible by the Tax Act, the reporting requirements, rules, and regulations will make some activities more time-consuming and costly. As a result, our management and other personnel will need to devote a substantial amount of time to remedy the identified material weaknesses and otherwise ensure that we comply with all of these requirements and to keep pace with new regulations, otherwise we may fall out of compliance and risk becoming subject to litigation or being delisted, among other potential problems.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly impact our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. Employees may also unintentionally or willfully disclose our proprietary and/or confidential information to competitors. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, including due to the impact of any potential new outbreaks related to the COVID-19 pandemic, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease office and laboratory space, which consists of approximately 5,000 square feet and 1,750 square feet located in Bala Cynwyd, PA and Philadelphia, PA, respectively. Our office lease expires in August 2023 with an option to extend the lease for an additional three years, and our laboratory lease expires in December 2020, with an option to extend the lease for an additional two years.

The Company is party to an operating lease for approximately 17,705 square feet of office space in Boston, Massachusetts (the "Boston Lease"). The Boston Lease expires in October 2029. On October 27, 2020, the Company entered into a sublease agreement whereby the Company subleased all 17,705 square feet of office space leased under the Boston Lease until October 2029.

The Company believes that it will need to increase both its office and laboratory facilities in the near term. We believe that both appropriate office and laboratory space will be readily available on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

We may be subject to other legal proceedings and claims in the ordinary course of business. We cannot predict the results of any such disputes, and despite the potential outcomes, the existence thereof may have an adverse material impact on us due to diversion of management time and attention as well as the financial costs related to resolving such disputes.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market Information

Our common stock is publicly traded on the Nasdaq Global Market under the symbol "LRMR."

Holders

As of March 1, 2021, the Company had approximately 29 record holders of its common stock.

Dividends

The Company has not declared or paid any dividends since its inception nor does it expect to pay dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

The information under the heading "Securities Authorized for Issuance Under Equity Compensation Plans" will be filed in the Company's definitive proxy statement for the 2021 annual meeting of stockholders and is incorporated herein by reference.

Recent Sales of Unregistered Securities

There have been no sales of unregistered securities other than as previously disclosed by the Company in our Current Reports on Form 8-K as filed with the SEC.

Issuer Purchases of Equity Securities

None.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Additionally, the Company has applied the amendment to Regulation S-K Item 301 which became effective on February 10, 2021 and therefore, will not be required to provide this information in future periods if the Company no longer qualifies as a smaller reporting company under Rule 12b-2.

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

You should read the following discussion and analysis of our financial condition and results of operations together with the section titled "Selected Consolidated Financial Data" and the consolidated financial statements and the related notes included elsewhere in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements based upon our current plans, expectations and beliefs that involve risks, uncertainties and assumptions. Our actual results may differ materially from those described in or implied by these forward-looking statements as a result of many factors, including those set forth under the section titled "Risk Factors" and in other parts of this Annual Report.

Overview

We are a clinical-stage biotechnology company focused on developing treatments for patients suffering from complex rare diseases using our novel cell penetrating peptide technology platform. Our lead product candidate, CTI-1601, is a subcutaneously administered, recombinant fusion protein intended to deliver human frataxin, or FXN, an essential protein, to the mitochondria of patients with Friedreich's ataxia. Friedreich's ataxia is a rare, progressive and fatal disease in which patients are unable to produce sufficient FXN due to a genetic abnormality. There is currently no effective therapy for Friedreich's ataxia. CTI-1601 is currently being evaluated in Phase 1 clinical trials in patients with Friedreich's ataxia. In December 2020, we announced the completion of dosing of a SAD trial of CTI-1601. A Safety Review Committee reviewed preliminary blinded data after each cohort of the placebo-controlled SAD clinical trial and recommended continuation of the trial. Based on preliminary data, single subcutaneous injections of CTI-1601 at doses up to 100 mg are thought to have been well tolerated. Injection site adverse events were mild and transient, and no serious adverse events were reported. Analysis of clinical trial results remains ongoing. We expect to complete our phase 1 MAD study in the first quarter of 2021, and we expect to release top line results of both studies in the second quarter of 2021.

We have received orphan drug status, fast track designation and rare pediatric disease designation, from the FDA, for CTI-1601. In addition, we received orphan drug designation for CTI-1601 from the European Commission. The receipt of such designations or positive opinions may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA or EMA procedures and does not assure ultimate approval by the FDA or EMA.

Our CPP technology platform, which enables a therapeutic molecule to cross a cell membrane in order to reach intracellular targets, has the potential to enable the treatment of other rare and orphan diseases. We intend to use our proprietary platform to target additional orphan indications characterized by deficiencies in or alterations of intracellular content or activity.

Since our inception, we have devoted substantially all of our resources to developing CTI-1601, building our intellectual property portfolio, developing third-party manufacturing capabilities, business planning, raising capital, and providing general and administrative support for such operations.

We have never generated any revenue and have, to date, incurred net losses. We incurred net losses of approximately $42.5 million and $23.1 million for the year ended December 31, 2020, and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $65.6 million and a cash, cash equivalents and marketable debt securities balance of $92.6 million. These losses have resulted principally from costs incurred in connection with research and development activities, and general and administrative costs associated with our operations. We expect to incur significant expenses and operating losses for the foreseeable future.

We expect to continue to incur expenses in connection with our ongoing activities, if and as we:

- Continue to advance the development of CTI-1601 through additional clinical trials;
- Seek to identify and advance development of additional product candidates into clinical development and seek new indications for our product candidates;

- Seek to obtain regulatory approval for our product candidates;
- Identify, acquire or in-license other product candidates and technologies;
- Maintain, leverage and expand our intellectual property portfolio; and
- Expand our operational, financial and management systems and personnel, including personnel to support our clinical development, our manufacturing operations and future commercialization efforts and our operations as a public company.

As a result, we will need additional financing to support our continuing operations. Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public equity, private equity, debt financings, or other sources, which may include collaborations with third parties. Arrangements with collaborators or others may require us to relinquish rights to certain of our technologies or product candidates. In addition, we may never successfully complete development of any of our product candidates, obtain adequate patent protection for our technology, obtain necessary regulatory approval for our product candidates or achieve commercial viability for any approved product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability and may never do so.

We believe that, based on our current operating plan, our cash and cash equivalents as of the date of this Annual Report will enable us to fund operations for at least twelve months from the issuance of our annual financial statements.

COVID-19 Update

In March 2020, the World Health Organization declared the outbreak of COVID-19, a novel strain of Coronavirus, a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads and mutates.

In December 2020, the FDA granted emergency use authorization for two COVID-19 vaccines. Additional Emergency Use Authorizations, or EUAs, are expected to be granted to other pharmaceutical/biotechnology companies. The distribution and administration of the two approved vaccines have been slow.

In January 2021, several mutations of the original COVID-19 virus were discovered. These variants are believed to be more contagious and perhaps more deadly than the original COVID-19 virus.

The extent of the effect of COVID-19 on our operational and financial performance will depend on future developments, including the duration, spread and intensity of the pandemic, including the spread of more contagious and deadly variants, the successful distribution and use of current and future COVID-19 vaccines, and governmental, regulatory and other private sector responses, all of which are uncertain and difficult to predict. Although we are unable to estimate the financial effect of the pandemic at this time, if the pandemic remains uncontained or if the current vaccines prove ineffective against future viral mutations, it could have a material adverse effect on our business, results of operations, financial condition and cash flows. The financial statements do not reflect any adjustments as a result of the pandemic.

The pandemic resulted in the temporary stoppage of our CTI-1601 Phase 1 clinical trials in patients with Friedreich’s ataxia. In July 2020, we resumed these clinical trials. We completed dosing of the SAD clinical trial in December 2020 and we expect to complete the dosing of the third cohort of the MAD clinical trial in the first quarter of 2021.

We conduct these clinical trials at one clinical trial site. Because Friedreich's ataxia is a rare disease, there are a limited number of patients in close proximity to the clinical trial site and clinical trial patients travel from locations throughout the United States to the clinical trial site to participate. After dosing, patients remain in isolation in the clinical research unit for a period of time. The travel advisories and risk of infection related to COVID-19 have presented increased risks to patients traveling to our clinical trial site for dosing and we expect to incur additional clinical trial costs to safely transport and isolate patients participating in the trial. In addition, additional stoppages or delays in the trial could result from new developments with respect to COVID-19. While top line results from the ongoing Phase 1 clinical trials were originally expected by the end of 2020, the delay in the clinical trial timeline caused by the ongoing impact of COVID-19 resulted in top line results now being expected in the second quarter of 2021. We may experience additional delays in clinical trial timelines as a result of additional travel and hospital restrictions related to the COVID-19 pandemic which may be imposed, including as a result of resurgences of COVID-19 cases in certain geographic areas.

Merger with Zafgen, Inc.

On December 17, 2019, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Zordich Merger Sub, Inc., or Merger Sub, our wholly owned subsidiary, Chondrial, and Chondrial Holdings LLC or Holdings, (the sole investor in Chondrial) pursuant to which the Merger Sub would merge with and into Chondrial, with Chondrial surviving the merger as our wholly owned subsidiary, or the Merger. The Merger was completed on May 28, 2020 pursuant to the terms of the Merger Agreement.

Pursuant to the terms of the Merger Agreement, upon closing of the Merger, all of Chondrial's outstanding common stock was exchanged for our common stock and all outstanding options exercisable for units of Holdings were exchanged for options to purchase our common stock. In addition, immediately prior to the closing of the Merger, we effected a 1 for 12 reverse stock split and changed our name from Zafgen, Inc. to Larimar Therapeutics, Inc. Following the Merger, the business conducted by Chondrial became our primary business.

The business combination was accounted for as a reverse acquisition in accordance with GAAP. Under this method of accounting, Chondrial was deemed to be the accounting acquirer for financial reporting purposes. This determination was primarily based on the facts that, immediately following the merger: (i) Chondrial's stockholders owned a substantial majority of the voting rights in the combined company, (ii) the majority of the board of directors of the combined company was composed of directors designated by Chondrial under the terms of the Merger Agreement and (iii) existing members of Chondrial management comprised the management of the combined company. Accordingly, for accounting purposes, the business combination was treated as the equivalent of Chondrial issuing stock to acquire Zafgen's net assets. As a result, as of the closing date of the Merger, Zafgen's net assets were recorded at their acquisition-date fair values, which were then adjusted for the difference between the purchase price and the fair value of the assets acquired, in the financial statements of Chondrial and the reported operating results prior to the business combination are those of Chondrial. As the Merger has been accounted for as an asset acquisition, goodwill has not been recorded within the consolidated balance sheet.

Private Placement

On May 28, 2020, we entered into a Securities Purchase Agreement with certain accredited investors for the sale by us in a private placement of 6,105,359 shares of our common stock, and pre-funded warrants to purchase an aggregate of 628,403 shares of our common stock, or the Pre-funded Warrants. The Pre-Funded Warrants are immediately exercisable at an exercise price for $0.01 and are exercisable indefinitely. We refer to this sale herein as the Private Placement.

The Private Placement closed on June 1, 2020. The aggregate gross proceeds for the issuance and sale of the Private Placement Shares and Pre-Funded common stock Warrants were $80.0 million and, after deducting certain of our expenses, the net proceeds we received in the Private Placement were $75.4 million. We intend to use the net proceeds from the Private Placement for research and development of our product candidates, working capital and general corporate purposes.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales, and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts result in clinical success and regulatory approval or collaboration agreements with third parties for our product candidates, we may generate revenue from those product candidates or collaborations.

Operating Expenses

The majority of our operating expenses since inception have consisted primarily of research and development activities, and general and administrative costs.

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- third-party contract costs relating to research, formulation, manufacturing, nonclinical studies and clinical trial activities;
- employee related costs, including salaries, benefits and stock-based compensation expenses for employees engaged in scientific research and development functions;
- external costs of outside consultants and vendors;
- payments made under our third-party licensing agreements;
- sponsored research agreements;
- laboratory consumables; and
- allocated facility-related costs.

Research and development costs are central to our business and are expensed as incurred. Costs for certain activities, such as manufacturing, nonclinical studies and clinical trials are generally recognized based on the evaluation of the progress of completion of specific tasks using information and data provided by our vendors and collaborators. We expect to increase our investment in research and development in order to advance CTI-1601 through additional clinical trials. As a result, we expect that our research and development expenses will increase throughout the foreseeable future as we pursue clinical development of CTI-1601 or any other product candidates we develop.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of CTI-1601 or any other product candidates we develop. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. The duration, costs, and timing of clinical trials and development of CTI-1601 or any other product candidates we develop will depend on a variety of factors, including:

- the scope, rate of progress and expense of clinical trials and other research and development activities, including the ongoing impact of COVID-19 on these activities;
- clinical trial results;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation;

- the timing and receipt of any regulatory approvals;
- the influence of the FDA or other regulatory authority on our clinical trial design;
- establishing manufacturing capabilities or making arrangements with third-party manufacturers and risk involved with development of manufacturing processes, FDA pre-approval inspection practices and successful completion of manufacturing batches for clinical development and other regulatory purposes;
- the impact of the on-going COVID-19 pandemic including the mutations of the original virus that may prove more contagious and deadly;
- our ability to obtain and maintain patent and trade secret protection and regulatory exclusivity for our product candidates; and
- our ability to retain key research and development personnel.

A change in the outcome of any of these variables with respect to the development of a product candidate could significantly change the costs, timing and viability associated with the development of that product candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, consisting of salaries, related benefits and stock-based compensation, of our executive, finance, information technology, and other administrative functions. General and administrative expenses also include the costs of functioning as a public company, specifically audit, directors and officers insurance and other professional and legal expenses, including corporate and intellectual property activities. General and Administrative expenses also include other insurance expenses, and professional fees for, tax and legal services, including legal expenses to pursue patent protection of our intellectual property. We expect that our general and administrative expenses will increase in the foreseeable future as we hire additional employees to implement and improve our operational, financial and management systems.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate these estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

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 and evaluate payments made to vendors in advance of actual work activities being performed. This process involves reviewing open contracts and purchase orders, communicating with our personnel and outside vendors 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. 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. Examples of estimated accrued research and development expenses include fees paid to:

- CROs, in connection with clinical trials;

- vendors in connection with nonclinical development activities;
- contract manufacturing organizations in connection with the production of preclinical and clinical trial materials; and
- vendors related to product candidate manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials and manufacturing costs on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs or CMOs that conduct and manage clinical trials or manufacture clinical trial material on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense, nonclinical expense or manufacturing activities. Payments under some of these contracts depend on factors such as the completion of milestones. In accruing CRO service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. In accruing CMO costs, we estimate the time period that manufacturing will be completed, the achievement of milestones and the percentage completion of each specific CMO agreement. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid 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 recognizing adjustments in future periods as additional information becomes available.

Stock-Based Compensation

We measure all stock-based awards granted to employees, non-employee consultants and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. Typically, we issue awards with only service-based vesting conditions and record the expense for these awards using the straight-line method. We account for forfeitures as they occur.

We classify stock-based compensation expense in our consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Prior to May 28, 2020, we had been a private company and lacked company-specific historical and implied volatility information for our common stock. Therefore, we estimate our expected common stock price volatility based on the historical volatility of publicly traded peer companies and expect to continue to do so until we have adequate historical data regarding the volatility of our own traded stock price. The expected term of our stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield considers the fact that we have never paid cash dividends on common stock and do not expect to pay any cash dividends in the foreseeable future.

Results of Operations

Comparison of the years ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		
	2020	2019	Increase (Decrease)
	(in thousands)		
Statement of Operations Data:			
Operating expenses:			
Research and development	$ 31,407	$ 20,790	$ 10,617
General and administrative	11,397	2,424	8,973
Total operating expenses	42,804	23,214	19,590
Loss from operations	(42,804)	(23,214)	(19,590)
Other income, net	322	82	240
Net loss	$ (42,482)	$ (23,132)	$ (19,350)

Research and development expenses

Research and development expenses for the year ended December 31, 2020 increased $10.6 million compared to the year ended December 31, 2019. The increase in research and development expenses as compared to the prior year period was primarily driven by higher clinical supply manufacturing costs of $3.3 million, an increase in clinical trial costs of $4.8 million, an increase in personnel related costs of $1.7 million due to headcount additions in our research and development functions and an increase in stock compensation expense of $0.7 million associated with stock option grants made in 2020. The remaining increase is primarily related to internal laboratory costs, increased facility costs partially offset by a decrease in toxicology studies costs.

General and administrative expenses

General and administrative expenses for the year ended December 31, 2020 increased $9.0 million compared to the year ended December 31, 2019. The increase in general and administrative expenses as compared to the prior year period was primarily driven by an increase in professional fees and insurance costs of $6.3 million that are mainly due to the costs of operating as a public company, an increase in personnel related costs of $0.7 million due to increased headcount, and an increase in stock-based compensation of $1.3 million associated with stock option grants made in 2020. The remaining increase is primarily related to additional facility costs related to leases entered in 2020.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue from any sources, including from product sales, and have incurred significant operating losses and negative cash flows from our operations. We have devoted substantially all of our resources to developing CTI-1601, building our intellectual property portfolio, developing third-party manufacturing capabilities, business planning, capital raising, and providing general and administrative support for such operations.

Cash Flows

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

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Net cash used in operating activities	$ (42,199)	$ (22,699)
Net cash provided by (used in) investing activities	17,090	(83)
Net cash provided by financing activities	93,587	19,395
Net increase in cash, cash equivalents and restricted cash	$ 68,478	$ (3,387)

Net cash used in operating activities

During the year ended December 31, 2020, operating activities used $42.2 million of cash, resulting from our net loss of $42.5 million, adjusted for noncash expenses of $2.3 million, and changes in our operating assets and liabilities of $2.0 million. Our net loss was primarily attributed to operating expenses of $42.8 million. The change in operating assets and liabilities was primarily due to an increase in accrued expense and prepaid expenses due to the growth in our operating activities and partially offset by a decrease in accounts payable due to the timing of invoice processing.

During the year ended December 31, 2019, operating activities used $22.7 million of cash, resulting from our net loss of $23.1 million, adjusted for noncash expenses of $0.2 million and changes in our operating assets and liabilities of $0.2 million. Our net loss was primarily attributed to operating expenses of $23.2 million.

Net cash provided by (used in) investing activities

During the year ended December 31, 2020, investing activities provided $17.1 million of net cash, resulting from $41.9 million of cash acquired from our merger with Zafgen and $1.0 million representing maturities and sales of marketable securities, which was offset by transaction costs associated with the Merger of $1.3 million, the purchase of $24.5 million in marketable securities and $0.1 million used for the purchase of equipment.

During the year ended December 31, 2019, investing activities used $0.1 million of cash for the purchase of property and equipment.

Net cash provided by financing activities

During the year ended December 31, 2020, financing activities provided $93.6 million of cash that was the result of proceeds from the sale of common stock of $75.6 million and capital contributions from related parties prior to the merger with Zafgen of $18 million. During the year ended December 31, 2019, net cash provided by financing activities of $19.4 million was the result of capital contributions from related parties of $19.4 million.

Operating Capital Requirements

CTI-1601 is currently in Phase 1 clinical development, therefore we expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that we will continue to incur expenses, if and as we seek to:

- Continue to advance the development of CTI-1601 through additional clinical trials, including the cost of clinical materials as well as manufacturing scale up costs;

- Seek to identify and advance development of additional product candidates into clinical development and indications for our product candidates;

- Seek to obtain regulatory approvals for our product candidates;
- Identify, acquire or in-license other product candidates and technologies;
- Maintain, leverage and expand our intellectual property portfolio; and
- Expand our operational, financial and management systems and personnel, including personnel to support our clinical development and future commercialization efforts and our operations as a public company.

We expect to continue to generate operating losses for the foreseeable future. We completed the Merger on May 28, 2020 which, upon closing, provided cash, cash equivalents, restricted cash and marketable debt securities of $42.9 million concurrent with the Private Placement which provided additional net proceeds of $75.4 million. In August 2020, the Company entered into an Equity Distribution Agreement, or the ATM Agreement, with an investment bank., in connection with the establishment of an "at-the-market" offering program under which the Company may sell up to an aggregate of $50,000,000 of shares of its common stock from time to time through this investment bank., as sales agent. As of December 31, 2020, 11,524 shares of common stock have been sold under the Agreement for net proceeds of $0.2 million at an average gross price per share of $21.89.

We believe that, based on our current operating plan, our cash, cash equivalents and marketable debt securities as of the filing date, we will be able to fund operations for at least twelve months.

Until such time, if ever, as we can generate substantial revenue, we expect to seek additional funding through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements, and other collaborations, strategic alliances and licensing arrangements. We may not be able to obtain financing on acceptable terms, or at all, and we may not be able to enter into collaborations or other arrangements. The terms of any financing may adversely affect the holdings or our existing stockholders' rights. If we are unable to obtain additional funding, we will be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which would adversely affect our business, or we may be unable to continue operations.

Off-Balance Sheet Arrangements

During the periods presented we did not have, and we currently do not have, any off-balance sheet arrangements, as defined under SEC rules, such as relationships with unconsolidated entities or financial partnerships, which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our balance sheets.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2020 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments due by Period				
	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(in thousands)				
Lease Obligations	$ 10,101	$ 1,296	$ 2,343	$ 2,148	$ 4,314
Total	$ 10,101	$ 1,296	$ 2,343	$ 2,148	$ 4,314

Recently Issued Accounting Pronouncements

Please read Note 2 to our consolidated financial statements included in Part , Item," of this Annual Report for a description of recent accounting pronouncements applicable to our business.

Other Company Information

None.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements and the report of our independent registered public accounting firm are included in this Annual Report on Form 10-K on the pages indicated in Part IV, Item 15.

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

Management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on their evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Financial Officer have concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Remediation of Previously Reported Material Weaknesses

A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis by the company’s internal controls. As previously reported on Form 8-K/A filed with the SEC on June 26, 2020 and in our subsequent Form 10-Q reports for the periods ending June 30 and September 30, 2020, management identified material weaknesses in internal control over financial reporting during the audit of our consolidated financial statements for the years ending December 31, 2019 and December 31, 2018. The material weaknesses that were previously identified related to the following:

- We did not maintain an effective control environment commensurate with our financial reporting requirements. We lacked a sufficient number of professionals with an appropriate level of accounting and controls knowledge, training and experience to appropriately analyze, record and disclose accounting matters timely, completely and accurately. Additionally, the limited personnel resulted in our inability to consistently establish appropriate authorities and responsibilities in pursuit of our financial reporting objectives, as demonstrated by, amongst other things, our insufficient segregation of duties in our finance and accounting functions. This material weakness contributed to the following material weakness.

- We did not design and maintain adequate controls over the preparation and review of certain account reconciliations and journal entries. Specifically, we did not design and maintain controls to ensure (i) appropriate segregation of duties in the preparation and review of account reconciliations and journal entries, and (ii) account reconciliations and journal entries were reviewed at the appropriate level of precision. This material weakness resulted in adjustments to prepaid expenses and accrued expenses which were identified and recorded as part of the audit of our consolidated financial statements as of and for the years ended December 31, 2019 and December 31, 2018.

Management has been actively engaged in remediating the above-described material weaknesses. During the year ended December 31, 2020, we implemented measures designed to improve our internal control over financial reporting to remediate these material weaknesses, including:

- Hiring a Chief Financial Officer with extensive public accounting and public company experience;
- Evaluating the corporate finance and accounting organization and hiring additional qualified accounting and finance personnel including financial consultants to enable the implementation of internal control over financial reporting including adequate segregation of duties among accounting and finance personnel;
- Engaging professional accounting consultants to assist management in the documentation of policies, procedures, and the identification, documentation, and evaluation of our internal control over financial reporting including testing the operating effectiveness of the organization's internal controls;
- Developing a risk assessment framework to identify and evaluate sources of potential risks to our financial statements and adding or modifying controls as needed to address such risks;
- Documenting the step-by-step processes and controls necessary to ensure appropriate segregation of duties in the preparation and the review of account reconciliations and journal entries at an appropriate level of precision;
- Enhancing documentation and controls supporting the account reconciliations and journal entries; and
- Providing increased oversight and review of the account reconciliations and journal entries by personnel with U.S. GAAP knowledge and experience.

Management has concluded that the actions taken to strengthen our internal control over financial reporting, as well as the results of our testing over the design and operating effectiveness of these controls remediated the previously identified material weaknesses as of December 31, 2020. However, 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 applicable policies, processes and documentation requirements may deteriorate.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control – Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2020.

Changes in Internal Control Over Financial Reporting

There have been no changes in the Company's internal control over financial reporting during the fiscal quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by Item 11 of Form 10-K is incorporated by reference to the information contained in our definitive proxy statement for the 2021 annual meeting of stockholders.

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 of Form 10-K is incorporated by reference to the information contained in our definitive proxy statement for the 2021 annual meeting of stockholders.

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

The information required by Item 12 of Form 10-K is incorporated by reference to the information contained in our definitive proxy statement for the 2021 annual meeting of stockholders.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by Item 13 of Form 10-K is incorporated by reference to the information contained in our definitive proxy statement for the 2021 annual meeting of stockholders.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by Item 14 of Form 10-K is incorporated by reference to the information contained in our definitive proxy statement for the 2021 annual meeting of stockholders.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) 1. Financial Statements

See Index to the Consolidated Financial Statements on page F-1 of this Annual Report.

2. Financial Statement Schedules

None, as all information required in these schedules is included in the Notes to the Consolidated Financial Statements.

3. Exhibits

Reference is made to the Exhibit Index below for a list of exhibits required by Item 601 of Regulation S-K to be filed as part of this Annual Report.

The following exhibits are being filed herewith:

EXHIBIT INDEX

* Filed Herewith
** Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit

Exhibit No.	Exhibit
2.1	Agreement and Plan of Merger, dated as of December 17, 2019, by and among Zafgen, Inc., Chondrial Therapeutics, Inc., Chondrial Therapeutics Holdings, LLC, and Zordich Merger Sub, Inc. (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed on December 18, 2019).
2.2	Amendment No. 1 to Agreement and Plan of Merger, dated as of March 6, 2020, by and among Zafgen, Inc., Chondrial Therapeutics, Inc, Chondrial Therapeutics Holdings, LLC, and Zordich Merger Sub, Inc. (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed on March 6, 2020).
3.1	Ninth Amended and Restated Certificate of Incorporation of Larimar Therapeutics, Inc. (formerly known as Zafgen, Inc.) (incorporated by reference to Exhibit 3.1 of the Company's Current Report on Form 8-K filed on June 24, 2014).
3.2	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Zafgen, Inc. related to the Reverse Stock Split, dated May 28, 2020 (incorporated by reference to Exhibit 3.1 of the Company's Current Report on Form 8-K filed on June 2, 2020).
3.3	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Zafgen, Inc. related to the Name Change, dated May 28, 2020 (incorporated by reference to Exhibit 3.1 of the Company's Current Report on Form 8-K filed on June 2, 2020).
3.4	Amended and Restated By-laws of Larimar Therapuetics, Inc. (formerly known as Zafgen, Inc.) (incorporated by reference to Exhibit 3.2 of the Company's Current Report on Form 8-K filed on June 24, 2014).
4.1	Form of Company Pre-funded Warrant to Purchase Common Stock by and among the Company and certain investors (incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed on June 2, 2020).
4.2*	Description of the Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934.
10.1	Larimar Therapeutics, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed on September 29, 2020).
10.2	Amended and Restated 2006 Stock Option Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 filed on June 18, 2014).

10.3	2014 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 filed on June 18, 2014).
10.4	Equity Distribution Agreement by and between the Company and Piper Sandler & Co. (incorporated by reference to Exhibit 1.2 of the Company's Registration Statement on Form S-3 filed on August 14, 2020).
10.5	Larimar Therapeutics, Inc. Form of Stock Option Grant Notice and Award Agreement (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed on September 29, 2020).
10.6	Securities Purchase Agreement, dated as of May 28, 2020, by and among the Company and the investors listed on the Schedule of Investors attached thereto (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed on June 2, 2020).
10.7	Registration Rights Agreement, dated as of June 1, 2020, by and among the Company and certain Investors (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed on June 2, 2020).
10.8	Registration Rights Agreement, dated as of June 8, 2020, by and among the Company and certain Investors (incorporated by reference to Exhibit 10.3 of the Company's Registration Statement on Form S-3 filed on June 26, 2020).
10.9	Form of Indemnification Agreement between the Company and its directors (incorporated by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed on June 2, 2020).
10.10	Employment Agreement, dated July 31, 2020, by and between the Company and Carole Ben-Maimon (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed on August 6, 2020).
10.11	Employment Agreement, dated June 1, 2020, by and between the Company and Michael Celano (incorporated by reference to Exhibit 10.4 of the Company's Current Report on Form 8-K filed on June 2, 2020).
10.12**	License Agreement, by and between the Company and Wake Forest University Health Sciences, effective as of November 30, 2016. (incorporated by reference to Exhibit 10.6 of the Company's Quarterly Report on Form 10-Q filed on August 14, 2020).
10.13**	Amendment 1 to License Agreement, by and between the Company and Wake Forest University Health Sciences, effective as of November 28, 2017 (incorporated by reference to Exhibit 10.7 of the Company's Quarterly Report on Form 10-Q filed on August 14, 2020).
10.14**	Amendment 2 to License Agreement, by and between the Company and Wake Forest University Health Sciences, effective as of March 29, 2019 (incorporated by reference to Exhibit 10.8 of the Company's Quarterly Report on Form 10-Q filed on August 14, 2020).
10.15**	License Agreement, by and between the Company and Indiana University Research and Technology Corporation, effective as of November 30, 2016 (incorporated by reference to Exhibit 10.9 of the Company's Quarterly Report on Form 10-Q filed on August 14, 2020).
10.16**	First Amendment to License Agreement, by and between the Company, the Trustee of Indiana University and Indiana University Research and Technology Corporation, effective as of August 16, 2019 (incorporated by reference to Exhibit 10.10 of the Company's Quarterly Report on Form 10-Q filed on August 14, 2020).
10.17	Notice of Substitute Option Grant between the Company and a certain Optionee (incorporated by reference to Exhibit 4.5 of the Company's Registration Statement on Form S-8 filed on June 26, 2020).
10.18**	Commercial Lease by and between the Company and Shigo Center Plaza Owner, LLC dated as of February 12, 2019 (incorporated herein by reference to Exhibit 10.4 of the Registrant's Form 10-Q filed on May 9, 2019).
10.19**	Sublease, dated October 27, 2020 by and between the Company and Massachusetts Municipal Association, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 30, 2020).
21.1*	Subsidiaries of Larimar Therapeutics, Inc.
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1*	Rule 13a-14(a)/15d-14(a) certification of Principal Executive Officer.
31.2*	Rule 13a-14(a)/15d-14(a) certification of Principal Financial Officer.
32.1*	Section 1350 certification, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document

101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

ITEM 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the Unincorporated Community of Bala Cynwyd, Commonwealth of Pennsylvania, on the 4th day of March 2021.

LARIMAR THERAPEUTICS, INC.

By: /s/ Carole Ben-Maimon
Name: Carole Ben-Maimon
Title: President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Carole Ben-Maimon Carole Ben-Maimon	President, Chief Executive Officer and Director (principal executive officer)	March 4, 2021
/s/ Michael Celano Michael Celano	Chief Financial Officer (principal financial and accounting officer)	March 4, 2021
/s/ Joseph Truitt Joseph Truitt	Chairman, Board of Directors	March 4, 2021
/s/ Peter Barrett Peter Barrett	Director	March 4, 2021
/s/ Frank E. Thomas Frank E. Thomas	Director	March 4, 2021
/s/ Jonathan Leff Jonathan Leff	Director	March 4, 2021
/s/ Thomas E. Hamilton Thomas E. Hamilton	Director	March 4, 2021
/s/ Thomas O. Daniel Thomas O. Daniel	Director	March 4, 2021

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Larimar Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Larimar Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders' equity (deficit) and of cash flows for the years then ended including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

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

Accrued Research and Development Expenses

As described in Notes 2 and 7 to the consolidated financial statements, the Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers. Within accrued expenses, total accrued research and development expenses amounted to $3.4 million as of December 31, 2020. As disclosed, management's process involves reviewing open contracts and purchase orders, communicating with personnel and outside vendors to identify

services that have been performed, and estimating the level of service performed and the associated costs incurred for the services when invoices or other notification of actual costs have not been received.

The principal considerations for our determination that performing procedures relating to accrued research and development expenses is a critical audit matter are the significant judgment by management in developing the estimates of accrued research and development expenses, which in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's estimates of the level of service performed and the associated costs incurred for the services when invoices or other notification of actual costs have not yet been received. As disclosed by management, a material weakness existed during the year related to this matter.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others, testing management's process for developing the estimates of accrued research and development expenses, which included (i) evaluating the reasonableness of management's estimates of the level of service performed and the associated costs incurred for the services when invoices or other notification of actual costs have not yet been received; and (ii) testing the completeness and accuracy of data used by management in accrued research and development expenses calculations by comparing amounts, on a test basis, to contracts and invoices. Evaluating the reasonableness of management's estimate of the level of service performed and the associated costs incurred involved assessing management's ability to reasonably estimate the level of service and associated costs by comparing such estimates to invoices received, provisions in the contracts and other evidence including communications the company received from third-party vendors.

/s/ PricewaterhouseCoopers LLP
Philadelphia, Pennsylvania
March 4, 2021

We have served as the Company's auditor since 2020.

LARIMAR THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 68,148	$ 1,009
Marketable debt securities	24,490	—
Prepaid expenses and other current assets	5,314	3,741
Total current assets	97,952	4,750
Property and equipment, net	1,040	274
Operating lease right-of-use assets	3,936	87
Restricted cash	1,339	—
Other assets	419	90
Total assets	$ 104,686	$ 5,201
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 2,634	$ 3,539
Accrued expenses	5,843	2,259
Operating lease liabilities, current	515	97
Total current liabilities	8,992	5,895
Operating lease liabilities	6,002	—
Total liabilities	14,994	5,895
Commitments and contingencies (See Note 9)		
Stockholders' equity:		
Preferred stock; $0.001 par value per share; 5,000,000 shares authorized as of December 31, 2020 and December 31, 2019; no shares issued and outstanding as of December 31, 2020 and December 31, 2019	—	—
Common stock, $0.001 par value per share; 115,000,000 shares authorized as of December 31, 2020 and December 31, 2019; 15,367,730 and 6,091,250 shares issued and outstanding as of December 31, 2020 and December 31, 2019, respectively	15	6
Additional paid-in capital	155,290	22,432
Accumulated deficit	(65,614)	(23,132)
Accumulated other comprehensive gain	1	—
Total stockholders' equity (deficit)	89,692	(694)
Total liabilities and stockholders' equity (deficit)	$ 104,686	$ 5,201

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

LARIMAR THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2020	2019
Operating expenses:		
Research and development	$ 31,407	$ 20,790
General and administrative	11,397	2,424
Total operating expenses	42,804	23,214
Loss from operations	(42,804)	(23,214)
Other income, net	322	82
Net loss	$ (42,482)	$ (23,132)
Net loss per share, basic and diluted	$ (3.57)	$ (3.80)
Weighted average common shares outstanding, basic and diluted	11,883,155	6,091,250
Comprehensive loss:		
Net loss	$ (42,482)	$ (23,132)
Other comprehensive loss:		
Unrealized gain on marketable debt securities	1	—
Total other comprehensive gain	1	—
Total comprehensive loss	$ (42,481)	$ (23,132)

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

LARIMAR THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Par Value				
Balances as of December 31, 2018	6,091,250	$ 6	$ 2,908	$ —	$ —	$ 2,914
Capital contributions from related party	—	—	19,395	—	—	19,395
Stock-based compensation expense	—	—	129	—	—	129
Net loss	—	—	—	(23,132)	—	(23,132)
Balances as of December 31, 2019	6,091,250	$ 6	$ 22,432	$ (23,132)	$ —	$ (694)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Par Value				
Balances as of December 31, 2019	6,091,250	$ 6	$ 22,432	$ (23,132)	$ —	$ (694)
Capital contributions from related party	—	—	17,995	—	—	17,995
Merger with Zafgen Inc.	3,124,337	3	37,116	—	—	37,119
Private Placement, net of transaction costs	6,105,359	6	74,844	—	—	74,850
Issuance of Common Stock to placement agent for advisory fees in lieu of cash and other issuances of common stock	46,784	—	742	—	—	742
Stock-based compensation expense	—	—	2,161	—	—	2,161
Unrealized gain on marketable debt securities	—	—	—	—	1	1
Net loss	—	—	—	(42,482)	—	(42,482)
Balances as of December 31, 2020	15,367,730	$ 15	$ 155,290	$ (65,614)	$ 1	$ 89,692

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

LARIMAR THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (42,482)	$ (23,132)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	2,161	129
Depreciation expense	155	78
Amortization of premium on marketable securities	10	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,647)	(3,285)
Accounts payable	(3,288)	2,630
Accrued expenses	3,232	945
Right-of-use assets	405	—
Operating lease liabilities	(427)	—
Other assets	(318)	(64)
Net cash used in operating activities:	(42,199)	(22,699)
Cash flows from investing activities:		
Purchase of property and equipment	(62)	(83)
Purchase of marketable securities	(24,486)	—
Maturities and sales of marketable securities	1,000	—
Cash, cash equivalents, and restricted cash acquired in connection with the Merger	41,934	—
Merger transaction costs	(1,296)	—
Net cash provided by (used in) investing activities	17,090	(83)
Cash flows from financing activities:		
Capital contribution from related party	17,995	19,395
Proceeds from sale of common stock and prefunded warrants, net of issuance costs	75,592	—
Net cash provided by financing activities	93,587	19,395
Net increase in cash, cash equivalents and restricted cash	68,478	(3,387)
Cash, cash equivalents and restricted cash at beginning of period	1,009	4,396
Cash, cash equivalents and restricted cash at end of period	$ 69,487	$ 1,009
Supplemental disclosure of non-cash investing and financing activities:		
Fair value of net assets acquired in the Merger, including $1.0 million of marketable debt securities and excluding cash acquired	$ (4,815)	$ —
Property and equipment included in accounts payable and accrued expenses	$ 460	$ —
Leased assets obtained in exchange for new operating lease liabilities	$ 448	$ —

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

1. Organization, Nature of the Business, COVID-19 Risk and Basis of Presentation

Larimar Therapeutics, Inc., together with its subsidiaries (the "Company" or "Larimar"), is a clinical-stage biotechnology company focused on developing treatments for patients suffering from complex rare diseases using our novel cell penetrating peptide technology platform. Our lead product candidate, CTI-1601, is a subcutaneously administered, recombinant fusion protein intended to deliver human frataxin, or FXN, an essential protein, to the mitochondria of patients with Friedreich's ataxia. Friedreich's ataxia is a rare, progressive and fatal disease in which patients are unable to produce sufficient FXN due to a genetic abnormality.

The Company is subject to risks and uncertainties common to pre-commercialization companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with governmental regulations, failure to secure regulatory approval for CTI-1601 or any other product candidates and the ability to secure additional capital to fund operations. Drug candidates currently under development will require extensive nonclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel, and infrastructure and extensive compliance-reporting capabilities. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

In March 2020, the World Health Organization declared the outbreak of COVID-19, a novel strain of Coronavirus, a global pandemic. This outbreak is causing major disruptions to businesses and markets worldwide as the virus spreads. The extent of the effect on the Company's operational and financial performance will depend on future developments, including the duration, spread and intensity of the pandemic, the impact of known and future variants of the COVID-19 virus, the effectiveness and availability of vaccines against all variants and mutations of the COVID-19 virus, the willingness of individuals to avail themselves of the vaccines, and governmental, regulatory and private sector responses, all of which are uncertain and difficult to predict. Although the Company is unable to estimate the financial effect of the pandemic at this time, if the pandemic remains uncontained or worsens, it could have a material adverse effect on the Company's business, results of operations, financial condition and cash flows. The financial statements do not reflect any adjustments as a result of the pandemic.

The pandemic resulted in the temporary stoppage of the Company's Phase 1 clinical trials studying CTI-1601 in patients with Friedreich's ataxia after the completion of two cohorts. In July 2020, the Company resumed its Phase 1 clinical trials of CTI-1601. The Company is conducting these clinical trials at one clinical trial site in New Jersey. Because Friedreich's ataxia is a rare disease, there are a limited number of patients in close proximity to the clinical trial site and clinical trial patients travel from throughout the United States to the clinical trial site to participate. After dosing, patients remain in isolation in the clinical research unit for a period of time. The travel advisories and risk of infection related to COVID-19 have presented increased risks to patients traveling to the Company's clinical trial site for dosing and the Company expects to incur additional clinical trial costs to safely transport and isolate patients participating in the trial. Top line data from these clinical trials are currently expected in the second quarter of 2021. The Company may experience delays in clinical trial timelines as a result of additional travel and hospital restrictions related to the COVID-19 pandemic which may be imposed, including as a result of resurgences of COVID-19 cases in certain geographic areas, the impact of the known and future virus variants, and the efficacy of vaccines against all variants and mutation of the COVID-19 virus.

Merger with Zafgen

On December 17, 2019, Zafgen, Inc. ("Zafgen"), Chondrial Therapeutics Inc. ("Chondrial"), Zordich Merger Sub, Inc. ("Merger Sub") and Chondrial Holdings, LLC ("Holdings"), the sole stockholder of Chondrial, entered into an Agreement and Plan of Merger, as amended on March 9, 2020 (the "Merger Agreement"), pursuant to which Merger Sub merged with and into Chondrial, with Chondrial surviving as a wholly owned subsidiary of the Company and the surviving corporation of the merger (the "Merger").

The transaction was accounted for as a reverse acquisition in accordance with accounting principles generally accepted in the United States of America ("GAAP"). Under this method of accounting, Chondrial was deemed to be the accounting acquirer for financial reporting purposes. This determination was primarily based on the facts that, immediately following the Merger: (1) former shareholders of Chondrial own a substantial majority of the voting rights of the post-merger company; (2) the majority of the board of directors of the combined company is composed of directors designated by Chondrial under the terms of the merger agreement; and (3) existing members of Chondrial management constitute the management of the combined company. Because Chondrial has been determined to be the accounting acquirer in the Merger, but not the legal acquirer, the Merger is deemed a reverse acquisition under the guidance of the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 805, *Business Combinations*. As a result, the historical financial statements of Chondrial are the historical financial statements of the combined company. As the Merger has been accounted for as an asset acquisition, goodwill has not been recorded within the consolidated balance sheet.

The Merger was completed on May 28, 2020 pursuant to the terms of the Merger Agreement. In addition, immediately prior to the closing of the Merger, Zafgen effected a 1-for-12 reverse stock split (the "Reverse Stock Split") of Zafgen's common stock, par value $0.001 per share (the "Zafgen Common Stock"). At the effective time of the Merger (the "Effective Time"), each share of Chondrial's common stock, par value $0.001 per share ("Chondrial Common Stock"), outstanding immediately prior to the Effective Time was converted into the right to receive shares of Zafgen Common Stock based on an exchange ratio set forth in the Merger Agreement. At the Effective Time following the Reverse Stock Split, the exchange ratio was determined to be 60,912.5005 shares of Zafgen Common Stock for each share of Chondrial Common Stock (the "Exchange Ratio"). At the closing of the Merger on May 28, 2020, Zafgen issued an aggregate of 6,091,250 shares of its common stock to Holdings (the "Merger Shares"), based on the Exchange Ratio after giving effect to the Reverse Stock Split described below. Holdings subsequently distributed the Merger Shares to its members.

In addition, all outstanding options exercisable for common units of Holdings became options exercisable for the shares of common stock of Zafgen based on the conversion factor discussed within the Merger Agreement. In connection with the Merger, Zafgen changed its name to Larimar Therapeutics, Inc. Following the closing of the Merger, Chondrial Therapeutics, Inc. became a wholly owned subsidiary of the Company. In December, Chondrial Therapeutics was legally merged into Larimar Therapeutics, Inc. As used herein, the words "the Company" refers to, for periods following the Merger, Larimar, together with its subsidiaries, and for periods prior to the Merger, Chondrial Therapeutics Inc., and its direct and indirect subsidiaries, as applicable.

Basis of Presentation

The consolidated financial statements include the accounts of Larimar and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated. The accompanying consolidated financial statements have been prepared in conformity with GAAP. Unless otherwise noted, all references to common stock share and per share amounts have also been adjusted to reflect the Exchange Ratio.

Reverse Stock Split

On May 28, 2020, immediately prior to the closing of the Merger, Zafgen effected the Reverse Stock Split. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect the Reverse Stock Split. No fractional shares were issued in connection with the Reverse Stock Split. Unless otherwise noted, all references to common stock share and per share amounts have also been adjusted to reflect the Exchange Ratio.

Going Concern Assessment

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, the Company has evaluated whether there are certain conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. As of the issuance date of these consolidated financial statements, the Company expects that its cash, cash equivalents and marketable securities will be sufficient to fund its forecasted operating expenses and capital expenditure requirements for at least the next twelve months from the issuance date of these financial statements.

Since its inception, the Company has incurred significant operating losses and negative cash flows from operations. The Company has incurred recurring losses since inception, including net losses of $42.5 million and $23.1 million for the years ended December 31, 2020, and 2019, respectively. In addition, as of December 31, 2020, the Company had an accumulated deficit of $65.6 million. The Company expects to continue to generate operating losses for the foreseeable future. As of December 31, 2020, we have approximately $92.6 million of cash, cash equivalents and marketable securities available for use to fund our operations.

The Company expects that its research and development and general and administrative expenses will continue to increase. The Company has not yet commercialized any products and does not expect to generate revenue from the commercial sale of any products for several years, if at all. Until such time, if ever, we expect to seek additional funding through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements, and other collaborations, strategic alliances and licensing arrangements. We may not be able to obtain financing on acceptable terms, or at all, and we may not be able to enter into collaborations or other arrangements.

If the Company is unable to obtain future funding when needed, the Company may be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or pre-commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. There is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all. Additionally, the terms of any financing may adversely affect the holdings or our existing stockholders' rights. In the event the Company is not successful in obtaining sufficient funding, the Company has discretion in delaying certain research and development programs and personnel expenses, which would provide further flexibility in managing liquidity.

The Company has funded its operations to date primarily with proceeds from sales of common stock, prefunded warrants for the purchase of common stock and contributions from Holdings. In 2020, the Company completed the Merger and acquired $42.9 million of cash, cash equivalents, restricted cash and marketable debt securities that were held by Zafgen immediately prior to the Merger. The Company also raised $75.4 million, net of offering costs, through a private offering of common stock and prefunded warrants to purchase shares of common stock in connection with and immediately after the closing of the Merger. In addition, in 2020, prior to the Merger, the Company received $18.0 million in capital contributions from Holdings.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expense, valuation of stock-based awards and valuation of leases. Due to inherent uncertainty involved in making estimates, actual results reported in future periods may be affected by changes in these estimates. On an ongoing basis, the Company evaluates its estimates and assumptions.

Concentrations of Credit Risk and Significant Suppliers

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents. The Company generally maintains cash balances in various operating accounts at financial institutions that management believes to be of high credit quality in amounts that may exceed federally insured limits. The Company has not experienced losses related to its cash and cash equivalents.

The Company is highly dependent on third-party manufacturers to supply products for research and development activities in its programs. The Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in these manufacturing services or in the supply of active pharmaceutical ingredients and formulated drugs.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents consisted of commercial paper, corporate bonds with maturity dates of less than three months at the date of acquisition and money market funds as of December 31, 2020. As of December 31, 2019, the Company did not have cash equivalents.

Marketable debt securities

Marketable debt securities consist of debt investments with original maturities greater than ninety days. The Company classifies its marketable debt securities as available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. When the fair value is below the amortized cost the amount of the expected credit loss is estimated. The credit-related impairment amount is recognized in net income; the remaining impairment amount and unrealized gains are reported as a component of accumulated other comprehensive income in stockholders' equity. Credit losses are recognized through the use of an allowance for credit losses account and subsequent improvements in expected credit losses are recognized as a reversal of the allowance account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, the allowance for credit loss is written off and the excess of the amortized cost basis of the asset over its fair value is recorded in net income.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over a five or seven-year estimated useful life for equipment, furniture and fixtures and office equipment. Leasehold improvements are amortized over the shorter of the asset life or the term of the lease agreement. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment, net, and the net operating lease asset. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. Any impairment loss, if indicated, is measured as the amount by which the carrying amount of the asset exceeds the estimated fair value of the asset.

Segment Information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company's focus is on the research, development and commercialization of novel therapeutics for the treatment of rare diseases.

Research and Development Costs

Costs associated with internal research and development and external research and development services, including drug development and nonclinical studies, are expensed as incurred. Research and development expenses include costs for salaries, employee benefits, subcontractors, facility-related expenses, depreciation, stock-based compensation, third-party license fees, laboratory supplies, and external costs of outside vendors engaged to conduct discovery, nonclinical and clinical development activities and clinical trials as well as to manufacture clinical trial materials, and other costs. The Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such prepaid expenses are recognized as an expense when the goods have been delivered or the related services have been performed, or when it is no longer expected that the goods will be delivered, or the services rendered.

Upfront payments, milestone payments and annual maintenance fees under license agreements are currently expensed in the period in which they are incurred.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-Based Compensation

The Company measures all stock-based awards granted to employees, non-employee consultants and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is the vesting period of the respective award. Typically, the Company issues awards with only service-based and market-based vesting conditions and records the expense for these awards using the straight-line method. The Company accounts for forfeitures as they occur.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Prior to May 28, 2020, the Company had been a private company and lacked company-specific historical and implied volatility information for its common stock. Therefore, the Company estimated its expected common stock price volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield considers the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2020 and 2019, the Company's only element of other comprehensive income was unrealized gain on marketable securities.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period. Basic shares outstanding includes the weighted average effect of the Company's prefunded warrants issued in June 2020, the exercise of which requires little or no consideration for the delivery of shares of common stock. Basic and diluted weighted average shares of common stock outstanding for the twelve months ended December 31, 2020 includes the weighted average effect of 628,403 prefunded warrants for the purchase of shares of common stock, which were issued in June 2020, and for which the remaining unfunded exercise price is $0.01 per share.

Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common shares, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and unvested restricted common shares, as determined using the treasury stock method. For periods in which the Company has reported net losses, diluted net loss per common share attributable to common stockholders is the same as basic net loss per common share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is antidilutive.

The Company excluded 2,008,902 and 0 options to purchase common stock, outstanding as of December 31, 2020 and 2019, respectively, from the computation of diluted net loss per share for the twelve months ended December 31, 2020 and 2019, respectively, because they had an anti-dilutive impact due to the net loss incurred for the periods.

Prior to the Merger the Company did not have options to purchase common stock or unvested restricted common stock to exclude from the calculation of earnings per share as all outstanding options were for common units of Holdings that upon the Merger converted into options exercisable for the shares of common stock of the Company.

Recently Issued and Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The FASB subsequently issued amendments to ASU 2016-13. This standard requires entities to estimate an expected lifetime credit loss on financial assets ranging from short-term trade accounts receivable to long-term financings and report credit losses using an expected losses model rather than the incurred losses model that was previously used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, the standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. This standard limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. The Company adopted the standard on January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. This standard modifies certain disclosure requirements on fair value measurements. This standard became effective for the Company on January 1, 2020. The adoption of this standard did not have a material impact on the Company's disclosures.

3. Merger Accounting

On May 28, 2020, the Company completed its merger with Zafgen. Based on the Exchange Ratio, immediately following the Merger, former Zafgen stockholders, Zafgen option holders and other persons holding securities or other rights directly or indirectly convertible, exercisable or exchangeable for Zafgen Common Stock (collectively, the "Zafgen Securityholders") owned approximately 34% of the outstanding capital stock of the combined company, and Holdings, the former Chondrial stockholder, owned approximately 66% of the outstanding capital stock of the combined company. At the closing of the Merger, all shares of Chondrial Common Stock were exchanged for an aggregate of 6,091,250 shares of Zafgen Common Stock, after giving effect to the Reverse Stock Split.

In addition, pursuant to the terms of the Merger Agreement, the Company assumed all outstanding stock options to purchase shares of Zafgen common stock at the closing of the Merger. At the closing of the Merger, such stock options became options to purchase an aggregate of 328,770 shares of the Company's common stock after giving effect to the Reverse Stock Split.

The total purchase price paid in the Merger has been allocated to the tangible and intangible assets acquired and liabilities assumed of Zafgen based on their fair values as of the completion of the Merger. Transaction costs primarily included bank fees and professional fees associated with legal counsel, auditors and printers. The following summarizes the purchase price paid in the Merger (in thousands, except share and per share amounts):

Number of shares of the combined organization owned by Zafgen stockholders(1)		3,124,337
Multiplied by the fair value per share of Zafgen common stock(2)	$	11.88
Fair value of consideration issued in effect of the Merger	$	37,119
Transaction costs	$	1,715
Purchase price:	$	38,834

(1) The number of shares of 3,124,337 represents the historical 37,492,044 shares of Zafgen common stock outstanding immediately prior to the closing of the Merger, adjusted for the Reverse Stock Split.

(2) Based on the last reported sale price of Zafgen common stock on the Nasdaq Global Market on May 28, 2020, the closing date of the Merger, and after giving effect to the Reverse Stock Split.

The allocation of the purchase price for the Merger was based on estimates of the fair value of the net assets acquired, which was then adjusted for the difference between the purchase price and the fair value of the assets acquired. The following summarizes the allocation of the purchase price to the net tangible and intangible assets acquired (in thousands):

Cash and cash equivalents	$	40,595
Marketable debt securities		1,014
Other current and noncurrent assets		357
Property and equipment, net		398
Restricted cash		1,339
Right-of-use asset		3,806
Current liabilities		(2,685)
Lease liability, net of current portion		(5,990)
Purchase price	$	38,834

4. Fair Value Measurements and Marketable Debt Securities

Fair Value Measurements

The Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2020 and December 31, 2019 are measured in accordance with the standards of ASC 820, *Fair Value Measurements and Disclosures*, which establishes a three-level valuation hierarchy for measuring fair value and expands financial statement disclosures about fair value measurements. The valuation hierarchy is based on upon the transparency of inputs to the valuation of an asset or liability as of the measurement date. The three levels are defined as follows:

Level – 1	Inputs to the valuation methodology are quoted prices (unadjusted) for identical assets or liabilities in active markets.
Level – 2	Inputs to the valuation methodology include quoted prices for similar assets and liabilities in active markets, and inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the financial instrument.
Level – 3	Inputs to the valuation methodology are unobservable and significant to the fair value measurement.

The Company's financial instruments consist primarily of cash and cash equivalents, accounts payable and accrued liabilities. For accounts payable and accrued liabilities, the carrying amounts of these financial instruments as of December 31, 2020 and December 31, 2019 were considered representative of their fair values due to their short term to maturity.

The following tables summarize the Company's cash equivalents and marketable debt securities as of December 31, 2020. There were no cash equivalents and marketable debt securities as of December 31, 2019:

	December 31, 2020			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Money market funds	$ 4,229	$ 4,229	$ —	$ —
Commercial paper	6,499	—	6,499	—
Corporate bonds	1,907	—	1,907	—
Total cash equivalents	12,635	4,229	8,406	—
Marketable securities:				
U.S Government securities	2,005	—	2,005	—
Commercial paper	22,485	—	22,485	—
Total marketable debt securities	24,490	—	24,490	—
Total cash equivalents and marketable debt securities	$ 37,125	$ 4,229	$ 32,896	$ —

Marketable Debt Securities

The following tables summarize the Company's marketable debt securities as of December 31, 2020. There were no marketable debt securities as of December 31, 2019:

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
Assets:				
U.S Government securities (due within 1 year)	$ 2,005	$ —	$ —	$ 2,005
Commercial paper (due within 1 year)	22,484	2	(1)	22,485
	$ 24,489	$ 2	$ (1)	$ 24,490

As of December 31, 2020, the Company did not have an allowance for credit losses. All investments with unrealized losses at December 31, 2020 have been in a loss position for less than twelve months or the loss is not material and were temporary in nature. The Company does not intend to sell the investments that are in an unrealized loss position before recovery of their amortized cost basis.

5. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31, 2020	December 31, 2019
	(in thousands)	
Prepaid research and development expenses	$ 4,460	$ 3,099
Prepaid insurance	571	$ 36
Payroll tax receivable	32	76
Capitalized transaction costs	—	419
Research and development tax credit sale receivable	—	82
Other prepaid expenses and other assets	251	29
	$ 5,314	$ 3,741

Capitalized transaction costs as of December 31, 2019 consists of capitalized legal and proxy fees incurred by the Company, related to the Merger. These costs were included in the purchase price allocation when accounting for the Merger.

6. Fixed Assets

Fixed assets, net consisted of the following:

	Useful Life	December 31, 2020	December 31, 2019
		(in thousands)	
Computer equipment	5 years	$ 66	$ 14
Lab equipment	5 years	849	389
Furniture and fixtures	7 years	460	50
		1,375	453
Less: Accumulated depreciation		(335)	(179)
		$ 1,040	$ 274

Depreciation expense was $0.2 million and $0.1 million for the years ended December 31, 2020 and 2019, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2020	December 31, 2019
	(in thousands)	
Accrued research and development expenses	$ 3,409	$ 1,295
Accrued payroll and related expenses	1,350	627
Accrued professional fees	924	337
Accrued other	160	—
	$ 5,843	$ 2,259

8. Stockholders' Equity and Stock Options

Common Stock and Prefunded warrants

As of December 31, 2020, the Company's Certificate of Incorporation, as amended and restated, authorized the Company to issue 115,000,000 of $0.001 par value common stock and 5,000,000 of $0.001 par value preferred stock. The voting, dividend and liquidation rights of the holders of the Company's common stock are subject to and qualified by the rights, powers and preferences of the holders of the preferred stock. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors of the Company (the "Board"), if any. No cash dividends have been declared or paid to date.

On May 28, 2020, the Company entered into a securities purchase agreement with certain accredited investors (the "Purchasers") for the sale by the Company in a private placement of 6,105,359 shares of the Company's common stock and prefunded warrants to purchase an aggregate of 628,403 shares of the Company's common stock, for a price of $11.88 per share of the common stock and $11.87 per prefunded warrant. The prefunded warrants are exercisable at an exercise price of $0.01 and will be exercisable indefinitely. The Purchasers may exercise the prefunded warrants on a cashless basis in the event that there is no effective registration statement covering the resale of the shares of common stock underlying the prefunded warrants on the date in which the Company is required to deliver the shares. The private placement closed on June 1, 2020. The aggregate gross proceeds for the issuance and sale of the common stock and prefunded warrants were $80.0 million; transaction costs totaled $4.6 million and resulted in net proceeds of $75.4 million. The Company's Registration Statement on Form S-3, filed with the SEC on June 26, 2020, registered the resale of 6,105,359 shares of common stock sold and the 628,403 shares of common stock underlying the prefunded warrants. MTS Health Partners served as placement agent to the Company in connection with the private placement. As partial compensation for these services, we issued MTS Health Partners 35,260 shares of common stock.

Equity Distribution Agreement

On August 14, 2020, the Company entered into an Equity Distribution Agreement (the "Agreement") with an investment bank, in connection with the establishment of an "at-the-market" offering program under which the Company may sell up to an aggregate of $50,000,000 of shares of common stock (the "ATM Shares") from time to time (the "Offering").

Under the Agreement, the Company will set the parameters for the sale of ATM Shares, including the number of ATM Shares to be issued, the time period during which sales are requested to be made, limitations on the number of ATM Shares that may be sold in any one trading day and any minimum price below which sales may not be made. Sales of the ATM Shares, if any, under the Agreement may be made in transactions that are deemed to be "at-the-market offerings" as defined in Rule 415 under the Securities Act. The Company will pay its investment bank a commission equal to 3.0% of the gross proceeds of any ATM Shares sold through the investment bank under the Agreement and will reimburse investment bank for certain specified expenses. The Agreement contains customary representations, warranties and agreements by the Company, indemnification obligations of the Company and its investment bank, other customary obligations of the parties and termination provisions. The Company has no obligation to sell any of the ATM Shares and may at any time suspend offers under the Agreement. As of December 31, 2020, 11,524 Shares of common stock have been sold under the Agreement for net proceeds of $0.2 million at an average gross price per share of $21.89.

Summary of Plans

Upon completion of the Merger with Zafgen, Zafgen's 2014 Stock Option and Incentive Plan (the "2014 Plan") and Zafgen's 2006 Stock Option Plan (the "2006 Plan" and together with the 2014 Plan the "Prior Plans") were assumed by the Company. As described below, the Company adopted a new equity incentive plan in July 2020 that was approved by the stockholders in September 2020. These three plans are administered by the Board or, at the discretion of the Board, by a committee of the Board.

2020 Equity Incentive Plan

The Company's Board of Directors adopted the 2020 Equity Incentive Plan (the 2020 Plan) on July 16, 2020 and the stockholders of the Company approved the 2020 Plan on September 29, 2020. The 2020 Plan replaces the 2014 Plan. Option outstanding under the Prior Plans will remain outstanding, unchanged and subject to the terms of the 2014 Plan and the respective award agreements, and no further awards will be made under the 2014 Plan.

However, if any award previously granted under the Prior Plans, expires, terminates, is canceled or is forfeited for any reason after the approval of the 2020 Plan, the shares subject to that award will be added to the 2020 Plan share pool so that they can be utilized for new grants under the 2020 Plan.

The 2020 Plan provides for the grant of incentive stock options ("ISOs"), nonstatutory stock options ("NSO"), stock appreciation rights, restricted stock awards, restricted stock unit awards, and cash or other stock-based awards. ISOs may be granted only to the Company's employees, including the Company's officers, and the employees of the Company's affiliates. All other awards may be granted to the Company's employees, including the Company's officers, the Company's non-employee directors and consultants, and the employees and consultants of the Company's affiliates.

As of December 31, 2020, 893,700 shares of common stock were available for grant under the 2020 Plan. The maximum number of shares that may be issued in respect of any awards under the 2020 Plan is the sum of: (i) 1,700,000 shares plus (ii) an annual increase on January 1, 2021 and each anniversary of such date thereafter through January 1, 2030, equal to the lesser of (A) 4% of the shares issued and outstanding on the last day of the immediately preceding fiscal year, and (B) such smaller number of shares as determined by the Board (collectively, the "Plan Limit"). The maximum aggregate number of shares that may be issued under the 2020 Plan in respect of incentive stock options is 8,000,000 over the ten-year term of the 2020 Plan. Subject to this provision, the Company added 614,709 shares available for grant to the 2020 Plan effective January 1, 2021 increasing the maximum number of shares of the Company's common stock that may be issued under the 2020 plan to 2,314,709 shares.

2014 Stock Option and Incentive Plan and 2006 Stock Option Plan

In 2014, the Board and stockholders of Zafgen adopted the 2014 Plan. The 2014 Plan provided for the grant of stock options, stock appreciation rights, restricted stock awards, restricted stock units, unrestricted stock awards, performance-share awards, cash-based awards and dividend equivalent rights to employees, members of the Board and consultants of the Company. The number of shares initially reserved for issuance under the 2014 Plan was 180,685 shares of common stock. As the 2020 Plan was adopted by the Company and approved by the Company's stockholders, no further awards will be made under the Prior Plans.

2016 Equity and Incentive Plan

Under the 2016 Equity Plan adopted by Holdings on November 30, 2016, (the "2016 Equity Incentive Plan"), the Board of Managers of Holdings (the "Board of Managers") or a committee thereof was authorized to issue 122,133 Common Units of Holdings or combination of Common Units, Common Unit options or profit interest units. On March 23, 2018, the Board of Managers increased the number of Common Units reserved for grant and issuance pursuant to the 2016 Plan from 122,133 to 138,133 and on April 29, 2019 increased the number of Common Units reserved for grant and issuance pursuant to the 2016 Plan by an additional 101,500 to 239,633. The Company has recorded costs incurred as stock-based compensation with a corresponding capital contribution from Holdings.

From January 1, 2020 through the Merger date Holdings did not issue options to purchase Common Units to employees of the Company. During the twelve months ended December 31, 2019 Holdings issued 73,986 options to purchase Common Units to employees of the Company.

The Company assumed all of the outstanding and unexercised options to purchase units of Holdings upon consummation of the Merger. Pursuant to the terms of the Merger Agreement, options to purchase 330,818 shares of the Company's common stock at a weighted average exercise price of $12.14 per share were substituted for the 202,392 options to purchase Common Units, with a weighted average exercise price of $10.36 per Common Unit, that were outstanding immediately prior to the Merger.

The Company treated the conversion as a modification pursuant to ASC 718, *Compensation—Stock Compensation,* and calculated the pre- and post-modification value of the options. The increase in fair value of the options was calculated to be $1.2 million. As $0.7 million related to vested options the expense was recognized immediately on the Merger date, and the remaining $0.5 million will be recognized over the remaining vesting term with the original grant date fair value remaining of $0.1 million.

Stock Valuation

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted to employees:

	2020	2019
Risk-free interest rate	0.37%	1.92%
Expected term (in years)	6.08	6.25
Expected volatility	91%	77%
Dividend yield	0.00%	0.00%

Stock Options

The following table summarizes the Company's stock option activity for the twelve months ended December 31, 2020 (amounts in millions, except for share and per share data):

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (a) (in millions)
Outstanding as of December 31, 2019	202,392	$ 10.36	7.5	$ —
Assumed as part of the Merger with Zafgen	328,770	74.80		
Modification of stock options	128,426	14.96		
Granted	1,356,074	12.34		
Forfeited	(6,760)	(77.63)		
Outstanding as of December 31, 2020	2,008,902	$ 22.31	7.9	$ 15.5
Exercisable as of December 31, 2020	585,152	$ 46.43	4.1	$ 2.6
Vested and expected to vest as of December 31, 2020	2,008,902	$ 22.31	7.9	$ 15.5

(a) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of the common stock for the options that were in the money at December 31, 2020.

2020 Option Grants

On July 16, 2020, the Company granted options to purchase 549,774 shares of common stock to employees under the 2014 Plan. The options have an exercise price equal to the closing stock price as of the grant date, and vest over four years, with 25% vesting on the first anniversary of the grant and the remainder vesting in equal monthly installments thereafter.

In addition, in 2020 the Company granted options to purchase 806,300 shares of common stock to employees and directors under the 2020 Plan. The options granted to employees have an exercise price equal to the closing stock price as of the grant date, and vest over four years, with 25% vesting on the first anniversary of the grant and the remainder vesting in equal monthly installments thereafter. The options granted to directors have an exercise price equal to the closing stock price as of the grant date, and vest monthly in equal installments over three years.

January 2021 Option Grants

On January 19, 2021, the Company granted options to purchase 280,150 shares of common stock to employees under the 2020 Plan. The options have an exercise price equal to the closing stock price as of the grant date, and vest over four years, with 25% vesting on the first anniversary of the grant and the remainder vesting in equal monthly installments thereafter.

Stock-Based Compensation

Stock-based compensation expense was classified in the consolidated statements of operations as follows:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Research and development	$ 788	$ 63
General and administrative	1,373	66
	$ 2,161	$ 129

As of December 31, 2020, total unrecognized compensation expense related to unvested stock options and restricted stock units was $13.5 million, which is expected to be recognized over a weighted average period of 3.45 years.

9. Commitments

Intellectual Property Licenses

The Company is party to a License Agreement (the "WFUHS License"), dated November 30, 2016 with Wake Forest University Health Sciences ("WFUHS") and a License Agreement (the "IU License"), dated November 30, 2016, as amended, with Indiana University ("IU"). Such agreements provide for a transferable, worldwide license to certain patent rights regarding technology used by the Company with respect to the development of CTI-1601.

In partial consideration for the right and license granted under these agreements, the Company will pay each of WFUHS and IU a royalty of a low single digit percentage of net sales of licensed products depending on whether there is a valid patent covering such products. As additional consideration for these agreements, the Company is obligated to pay each of WFUHS and IU certain milestone payments of up to $2.6 million in the aggregate upon the achievement of certain developmental milestones, commencing on the enrollment of the first patient in a Phase 1 clinical trial. The Company will also pay each of WFUHS and IU sublicensing fees ranging from a high single digit to a low double-digit percentage of sublicense consideration depending on the Company's achievement of certain regulatory milestones as of the time of receipt of the sublicense consideration. The Company is also obligated to reimburse WFUHS and IU for patent-related expenses. In the event that the Company disputes the validity of any of the licensed patents, the royalty rate would be tripled during such dispute. The Company is also obligated to pay to IU a minimum annual royalty of less than $0.1 million per annum starting in the 2020 calendar year for the term of the agreement.

In the event that the Company is required to pay IU consideration, then the Company may deduct 20% of such IU consideration on a dollar-for-dollar basis from the consideration due to WFUHS. In the event that the Company is required to pay WFUHS consideration, then the Company may deduct 60% of such WFUHS consideration on a dollar-for-dollar basis from the consideration due to IU.

During the twelve months ended December 31, 2020 and 2019, no milestones were achieved and no expense was recognized. Both agreements continue from their effective date through the last to expire of the licensed patents unless earlier terminated by either party.

Leases

On August 8, 2019, the Company entered into an operating lease for office space in Bala Cynwyd, Pennsylvania, effective as of December 15, 2019, for a period of three years and six months with an option to extend the lease for three additional years. Due to required tenant improvements to be completed by the landlord, the Company did not take immediate possession of the leased property and the lease term commenced on February 15, 2020. In the quarter ended March 31, 2020, the Company recorded an operating lease right-of-use asset and operating lease liability of $0.4 million.

On May 28, 2020, as part of the Merger with Zafgen, the Company acquired a non-cancellable operating lease for approximately 17,705 square feet of office space (the "Premises"). The lease expires on October 30, 2029. As part of the agreement, the Company is required to maintain a letter of credit, which upon signing was $1.3 million and is classified as restricted cash within the consolidated financial statements. In addition to the base rent, the Company is also responsible for its share of operating expenses, electricity and real estate taxes, which costs are not included in the determination of the leases' right-of-use assets or lease liabilities. The right-of-use asset is being amortized to rent expense over the remaining lease term. On October 27, 2020, the Company entered into a sublease agreement (the "Sublease") with Massachusetts Municipal Association, Inc. (the "Subtenant"), whereby the Company subleased the entire Premises to the Subtenant. The term of the Sublease commenced on the December 4, 2020 and continues until October 30, 2029. In connection with this sublease, we evaluated the need for impairment under ASC 360 and determined that there was no impairment.

The Sublease provides for an initial annual base rent of $0.8 million, which increases annually up to a maximum annual base rent of $1.0 million. The Subtenant also is responsible for paying to the Company future increases in operating costs (commencing on January 1, 2022), future increases in annual tax costs (commencing July 1, 2021) and all utility costs (commencing March 1,2021) attributable to the Premises during the term of the Sublease. As part of the Sublease, the subtenant deposited a letter of credit in the amount of $0.8 million to assure their performance under the sublease. If there are no uncured events of default under the sublease, the amount of this security deposit decreases over time to $0.4 million on the sixth anniversary of the Sublease.

On November 5, 2018, the Company entered into an operating lease for office and lab space in Philadelphia, Pennsylvania, effective as of January 1, 2019, and expiring on December 31, 2020 with an option to extend the lease for each of the two additional years. On August 4, 2020, the Company executed the first option to extend the lease for an additional year, expiring on December 31, 2021. We have determined this lease extension qualifies as a short-term lease, as the remaining renewal option is not considered reasonably certain, for which we have applied the accounting policy election to not record the related right-of-use asset and lease liabilities.

Expense arising from operating leases was $0.7 million and less than $0.1 million during the twelve months ended December 31, 2020 and 2019, respectively. For operating leases, the weighted-average remaining lease term for leases at December 31, 2020 and December 31, 2019 was 8.6 and 3.3 years, respectively. For operating leases, the weighted average discount rate for leases at December 31, 2020 and December 31, 2019 was 11.0% and 12.0%, respectively. The Company has not entered into any financing leases.

Maturities of lease liabilities due under these lease agreements as of December 31, 2020 are as follows:

Year Ending December 31, (in thousands)	Operating Leases
2021	$ 1,177
2022	1,197
2023	1,146
2024	1,065
Thereafter	5,397
Total lease payments	9,982
Less: imputed interest	(3,465)
Present value of lease liabilities	$ 6,517

10. Income Taxes

During the years ended December 31, 2020, and 2019, the Company recorded no income tax benefits for the net operating losses incurred in each year due to its uncertainty of realizing a benefit from those items.

The domestic and foreign components of loss before income taxes are as follows.

	Years ended December 31,	
	2020	2019
Domestic	$ (42,608)	$ (23,182)
Foreign	126	—
	$ (42,482)	$ (23,182)

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

	Year Ended December 31,	
	2020	2019
Federal statutory income tax rate	21.0%	21.0%
State taxes, net of federal benefit	7.8	7.9
Federal and state research and development tax credit	13.5	0.0
Nondeductible permanent differences	(0.2)	0.1
Change in deferred tax asset valuation allowance	(42.1)	(29.0)
Effective income tax rate	0.0%	0.0%

Net deferred tax assets as of December 31, 2020 and 2019 consisted of the following:

	2020	2019
Deferred tax assets:		
Capitalized R&D Expenses	$ 73,014	$ —
Stock Based Compensation	490	—
Net operating Loss Carryforwards	32,081	10,983
Tax credit carryforwards	8,904	62
Other Temporary Differences	50	690
Fixed Assets & Intangibles	75	—
Operating Lease Liability	1,786	—
Total deferred tax assets	$ 116,400	$ 11,735
Deferred tax liabilities:		
Operating Right of Use Asset	(1,081)	—
Total deferred tax liabilities	$ (1,081)	$ —
Less: Valuation allowance	$ (115,319)	$ (11,735)
Net deferred tax assets / (liabilities)	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2020 and 2019 related primarily to deferred tax assets acquired as a result of the Merger with Zafgen, increase in net operating loss carryforwards, and tax credit carryforwards and were as follows:

	Years ended December 31,	
	2020	2019
Valuation allowance as of the beginning of the year	$ 11,735	$ 5,300
Increases acquired as a result of the Merger with Zafgen	85,689	—
Increases recorded to income tax provision	17,895	6,435
Valuation Allowance at end of Year	$ 115,319	$ 11,735

As of December 31, 2020, the Company had net operating loss carryforwards that expire for federal, foreign and state income tax purposes of $113.2 million, $1.2 million and $113.2 million, respectively. The federal and state operating losses begin to expire in 2026 and 2030, while the foreign net loss carryforward can be carried forward indefinitely. As of December 31, 2020, the Company had federal net operating loss carryforwards that were generated after December 31, 2017 of $74.0 million that do not expire, however these carryforwards are limited to 80% of the taxable income in any one tax period. As of December 31, 2020, the Company also had available tax credit carryforwards for federal and state income tax purposes of $8.9 million which begin to expire in 2039. Utilization of the pre-Merger net operating loss carryforwards attributable to Zafgen, of approximately $33.5 million, are subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes occurred during the tax year associated with the Merger. In addition to the limitation of the pre-Merger NOL's of Zafgen, the net capitalized R&D deferred tax assets in the amount of $73.0 million is subject to the built-in loss rules under Section 382 and may not be realized if the underlying asset associated with the R&D is disposed within five years of the Merger, or May 28, 2025. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The ownership changes will limit the amount of pre-merger Zafgen carryforwards that can be utilized annually to offset future taxable income with an annual limitation of approximately $35 thousand per year. The Company has reduced their NOL and R&D tax credit deferred tax assets associated with the pre-Merger Zafgen operations as a result of the 382 analysis.

The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception associated with the pre-Merger Chondrial tax attributes. If the Company experienced a change of control, as defined by Section 382, at any time since inception, utilization of the pre-Merger Chondrial net operating loss carryforwards or tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or tax credit carryforwards before utilization. Further, until a study is completed, and any limitation is known, no amounts are being presented as an uncertain tax position.

As of December 31, 2020 and 2019, the Company's net deferred tax asset balance before the valuation allowance was $115.3 million and $11.7 million, respectively, and was comprised principally of net operating loss carryforwards, capitalized research and development expenses and tax credit carryforwards. During the years ended December 31, 2020, and 2019, gross deferred tax assets increased due to deferred tax assets acquired as a result of the Merger with Zafgen, additional net operating loss carryforwards, research and development tax credits generated.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2020 and 2019. Management reevaluates the positive and negative evidence at each reporting period.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 and 2019. The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal

course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending income tax examinations. The Company's tax years are still open under statute from 2016 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

11. Related Party Transactions

In November 2016, the Company entered into a consulting agreement with Mark Payne, M.D (the "Consulting Engagement"). Dr. Payne was a director of Chondrial at that time, a full-time employee of IU and one of the inventors of the licensed IU intellectual property, and as such is entitled to a certain share of the revenues received by IU under the IU License. Pursuant to the terms of his consulting agreement the Company agreed to pay Dr. Payne $0.1 million per year over the term of the agreement and granted Dr. Payne 123,853 restricted Common Units in Holdings. On November 30, 2016, 30% vested and was associated with Chondrial Therapeutics IP, LLC ("IP LLC") becoming a subsidiary of Holdings, which subsequently contributed to the Company on December 31, 2018. The remaining 70% is associated with future services (see Note 8) vesting ratably over 48 months beginning on December 1, 2016. The consulting agreement has a four-year term, subject to earlier termination. On November 30, 2020, The Company entered into a 1-month extension of the Consulting Engagement, expiring on December 31, 2020. During the twelve months ended December 31, 2020 and 2019, the Company recognized $0.1 million, related to this consulting agreement, recorded as research and development expense in the Statement of Operations. On January 1, 2021, the Company entered into a new consulting agreement with Mark Payne, M.D. which extended the term of the Consulting Engagement for a four-year term beginning on January 1, 2021.

The funding to the Company originated from Holdings' sale of Series A Preferred Units and Series B convertible preferred units with Deerfield Private Design Fund IV, L.P., Deerfield Private Design Fund III, L.P. and Deerfield Health Innovations Fund, L.P. (together, the "Deerfield Funds"), and certain other purchasers, from inception through May 28, 2020 and the contribution of the proceeds received by Holdings on such sales to the Company in order to fund the Company's operations.

Under a November 30, 2016 Series A Preferred Unit Purchase Agreement, as amended on September 8, 2017, November 15, 2017, November 14, 2018 and April 29, 2019, Holdings sold Series A Preferred Units for gross proceeds of $35.6 million. The gross proceeds were then contributed to the Company.

On November 21, 2019 (as amended on December 20, 2019), Holdings entered into a Second Amended and Restated LLC Agreement and entered into a Series B Bridge Unit Purchase Agreement with the Deerfield Funds and certain other purchasers to sell Series B convertible preferred units ("Series B Bridge Units") for gross proceeds of up to $10.0 million. The gross proceeds were then contributed to the Company.

On January 16, 2020, Holdings entered into a Third Amended and Restated LLC Agreement and entered into a Second Series B Bridge Unit Purchase Agreement with the Deerfield Funds and certain other purchasers to sell Second Series B convertible preferred units ("Second Series B Bridge Units") for gross proceeds of up to $15.0 million. The gross proceeds were contributed to the Company.

During the twelve months ended December 31, 2020 and 2019, Holdings provided the Company non-interest bearing, permanent funding from the above Series A and Series B preferred unit transactions, totaling $18.0 million and $19.4 million, respectively, which has been recorded as capital contributions with the balance of combined equity and additional paid in capital on the consolidated balance sheets and consolidated statements of changes in stockholders' equity for each respective period. No contributions were made by Holdings subsequent to the Merger.

In December 2020, the Company purchased a piece of laboratory equipment for $0.5 million from a supplier that one of our Board members is also a member of this supplier's board of directors. This purchase was billed at market rates with market payment terms.

DESCRIPTION OF THE COMPANY'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

Larimar Therapeutics, Inc., or the Company, has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The Company's common stock, $0.001 par value per share, or the Common Stock, is registered under Section 12(b) of the Exchange Act. The following description of our Common Stock is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Ninth Amended and Restated Certificate of Incorporation, as amended, or the Charter, and our Amended and Restated Bylaws, or the Bylaws, each of which is incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.2 is a part. We encourage you to read our Charter, Bylaws and the applicable provisions of the General Corporation Law of the State of Delaware, or the DGCL, for additional information.

Common Stock

Authorized Capital Stock. Our authorized capital stock consists of 115,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share.

Voting Rights. Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of our common stock do not have any cumulative voting rights.

Dividends. Holders of our common stock are entitled to receive ratably any dividends declared by our Board of Directors, or Board, out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock.

No Preemptive or Similar Rights. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions. In the event of a liquidation, dissolution or winding up of us, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing. Our common stock is listed on The Nasdaq Global Market under the symbol "LRMR."

Reverse Split

On May 28, 2020, we filed an amendment to our Charter in order to effect a 1-for-12 reverse stock split of our common stock effective for trading purposes on May 29, 2020. The number of authorized stock remained unchanged at 120,000,000 shares.

Preferred Stock

Our Board currently has the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock by us could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon a liquidation of us. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of us or other corporate action. No shares of preferred stock are outstanding, and we have no present plans to issue any shares of preferred stock.

Provisions of Our Charter and Bylaws and Delaware Anti-Takeover Law

Certain provisions of the DGCL and of our Charter and Bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our Board. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Board Composition and Filling Vacancies. Our Charter provides for the division of our Board into three classes serving staggered three-year terms, with one class being elected each year. Our Charter also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our Board, however occurring, including a vacancy resulting from an increase in the size of our Board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No Written Consent of Stockholders. Our Charter provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders. Our Charter and Bylaws provide that only a majority of the members of our Board then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our Bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements. Our Bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our Bylaws specify the requirements as to form and content of all stockholders' notices.

Amendment to Charter and Bylaws. As required by the DGCL, any amendment of our Charter must first be approved by a majority of our Board, and if required by law or our Charter, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our Charter must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our Bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the Bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our Board recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

As a Delaware corporation, we are also subject to provisions of Delaware law, including Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a

business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation any conflicts or violations of each party's agreements as a result of the merger or the merger agreement;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Exclusive Jurisdiction of Certain Actions. Our Charter provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our Charter or our Bylaws, or (iv) any action asserting a claim against us governed by the internal affairs doctrine. This provision does not apply to claims arising under the Exchange Act or the Securities Act. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar exclusive forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could rule that this provision in our Charter is inapplicable or unenforceable.

Exhibit 21.1

LIST OF SUBSIDIARIES

Subsidiary	Ownership Percentage	Jurisdiction of Incorporation or Organization
Zafgen Australia Pty Ltd.	100%	Australia
Chondrial Therapeutics IP, LLC	100%	Delaware
Zafgen Securities Corp.	100%	Massachusetts
Zafgen Animal Health, LLC	100%	Delaware

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-239510, 333-246370, and 333-228328) and Form S-8 (Nos. 333-239509 and 333-249287) of Larimar Therapeutics, Inc. of our report dated March 4, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Philadelphia, Pennsylvania
March 4, 2021

Exhibit 31.1

CERTIFICATION

I, Carole S. Ben-Maimon, M.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-K of Larimar 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.

Date: March 4 2021
/s/ Carole S. Ben-Maimon, M.D.
Carole S. Ben-Maimon, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Michael Celano, certify that:

1. I have reviewed this Quarterly Report on Form 10-K of Larimar 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.

Date: March 4 2021
/s/ Michael Celano
Michael Celano
Chief Financial Officer
(Principal Financial Officer and Accounting Officer)

Exhibit 32.1

CERTIFICATION
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
(Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Larimar Therapeutics, Inc. (the "Company"), does hereby certify, to the best of such officer's knowledge, that:

(1) The Quarterly Report on Form 10-K for the period ended December 31, 2020 (the "Report") of the Company 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 4, 2021

/s/ Carole S. Ben-Maimon, M.D.
Carole S. Ben-Maimon, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 4, 2021

/s/ Michael Celano
Michael Celano
Chief Financial Officer
(Principal Financial and Accounting Officer)