2020 ANNUAL REPORT

Dear Shareholders,

While the past year has been a period of change for Catabasis, our commitment to bringing hope with life-changing therapies to patients and families remains the same. We recently acquired Quellis Biosciences, including our lead program QLS-215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in preclinical development for the treatment of hereditary angioedema (HAE). We are excited about what the future holds for our company.

Last year, we completed the Phase 3 PolarisDMD trial of edasalonexent in Duchenne muscular dystrophy. Unfortunately, in October we announced that the trial did not meet its primary or secondary endpoints. Based on these results, we made the difficult decision to stop activities related to the development of edasalonexent. We are incredibly grateful for the Duchenne community and their support for edasalonexent through the years.

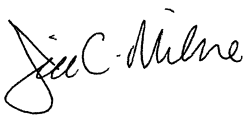
Following these disappointing results, we explored and evaluated strategic options with a financial advisor. As a result of our evaluation, in January 2021, we acquired Quellis Biosciences and announced a concurrent private placement, which closed on February 1, 2021, that resulted in gross proceeds of approximately $110.0 million, before deducting placement agent and other offering expenses. We believe that the acquisition represents an opportunity to create substantial value for our shareholders, while potentially providing benefit to a patient population with high disease burden.

HAE is a rare, debilitating and potentially life-threatening disease. While treatment options for HAE have improved, there remains unmet medical need, and the global market for HAE is strong and growing. Our vision for QLS-215, a monoclonal antibody inhibitor of plasma kallikrein, is that it will be a prophylactic treatment with infrequent dosing for patients affected by HAE. QLS-215 is currently in preclinical development and we expect to submit an Investigational New Drug Application in the first half of 2022 and plan to initiate a Phase 1a clinical trial with initial results anticipated by the end of 2022. Subsequently, assuming positive data from the Phase 1a clinical trial, we plan to initiate a Phase 1b/2 trial in patients with HAE in 2023 with initial results anticipated by the end of 2023. We believe that each of these clinical trials has the opportunity to demonstrate proof of concept for the differentiated profile of QLS-215.

Beyond QLS-215, we also acquired from Quellis a second undisclosed preclinical program, which we plan to evaluate and share more about later this year. As we look to the future, we intend to diversify and further build our pipeline and expand our commitment to improving the lives of patients and families.

Thank you for your support through this challenging year. We believe that the acquisition of Quellis and the private placement have put us in a strong position to accomplish our goals in 2021 and the coming years. We are excited about the new direction for Catabasis as we turn our focus to QLS-215 as a potential treatment for HAE as well as the long-term growth of our organization. We look forward to sharing more in the coming months, and we are appreciative of your confidence in Catabasis.

Sincerely,



Jill C. Milne, Ph.D.
Chief Executive Officer
April 20, 2021

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

or

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

For the transition period from to

Commission File Number: 001-37467

Catabasis Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-3687168**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
100 High Street Floor 28 Boston, Massachusetts	**02110**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(617) 349-1971**

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, $0.001 par value per share	**CATB**	**Nasdaq Global Market**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 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 ☒

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 30, 2020: $101,269,279

As of March 4, 2021, there were 23,417,006 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2021 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The registrant intends to file such proxy statement with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this Annual Report on Form 10-K relates.

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Summary of the Material Risks Associated with Our Business

Investing in our common stock involves a high degree of risk because our business is subject to numerous risks and uncertainties. The principal factors and uncertainties that make investing in our common stock risky include, among others:

- We are heavily dependent on the success of our product candidate, QLS-215 for the treatment of hereditary angioedema ("HAE"), which is in the pre-clinical stage of development, and has only produced results in pre-clinical and non-clinical settings. We cannot give any assurance that we will generate clinical or other data for QLS-215 or for any other future product candidates that is consistent with its pre-clinical data or sufficiently supportive to receive regulatory approval, which will be required before they can be commercialized.
- We will need substantial additional funding. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights.
- Our ability to continue as a going concern, if our stockholders do not approve the conversion of our Series X Preferred Stock into common stock.
- Our acquisition of Quellis Biosciences, Inc., or Quellis, involves numerous risks, including the inability to effectively integrate the QLS-215 program and other Quellis programs into our operations or realize the expected benefits from the acquisition, which could materially harm our operating results.
- We have never generated any revenue from product sales and may never be profitable.
- We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any future product candidate we may seek to develop.
- Clinical trials are costly, time consuming, difficult to enroll and inherently risky, and we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.
- QLS-215 or any future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial viability of an approved label, or result in significant negative consequences following marketing approval, if any.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results.
- We will need to maintain a cell line for QLS-215 and any other future biologic candidate that generates sufficient material for pre-clinical, non-clinical and clinical studies, and also build and maintain sufficient pre-clinical, clinical and commercial manufacturing drug substance and drug product capacity, in each case, through third party manufacturers, for QLS-215 and any other future product candidate that advances into such stages, on the timetables and in a manner that, in each case, are consistent with our expected development timetables and financial projections, the failure of which could materially harm our operating results and require us to raise capital sooner than we expect.
- Our forecasts of cash usage and how long our existing cash, cash equivalents and short-term investments may fund operating expenses may not be accurate and we may therefore use our cash, cash equivalents and short-term investments more rapidly than we expect, which could force us to delay, reduce or eliminate our product development programs or commercialization efforts, if any, and therefore materially harm our operating results, and we could be required to raise capital sooner than we expect.

- We have historically incurred losses, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future.
- The current pandemic of the novel coronavirus, or COVID-19, and the future outbreak of other highly infectious or contagious diseases, could seriously harm our development efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.
- The price of our stock may be volatile, and investors could lose all or part of their investment.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section entitled "Risk Factors" and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

These forward-looking statements include, among other things, statements about:

- our expectations regarding the timing of our planned filing of an initial investigational new drug application, or IND, for QLS-215, and the timing, nature, goals and results of our planned Phase 1a and Phase 1b/2 clinical trials of QLS-215, including that favorable results from such trials could establish proof of concept for the differentiation of QLS-215 as a potential treatment for HAE;
- our expectations about the unmet medical need for HAE, the potential differentiating attributes of QLS-215 as a potential treatment for HAE, along with the potential market impact of such differentiation, the potential of QLS-215 to be a best-in-class treatment for HAE, and the nature and anticipated growth of the global HAE market and HAE therapies;
- our expectations that the acquisition of Quellis may be an opportunity to create significant stockholder value;
- our expectations that we have identified a cell line for QLS-215 and the ability of such cell line to generate sufficient material for our planned QLS-215 toxicology studies and the master cell bank, and our plans and timetable for initiating current Good Manufacturing Practices, or cGMP, manufacturing of QLS-215;
- our expectations regarding our ability to expand our pipeline;
- the potential benefits of any future acquisition, in-license, collaboration or pre-clinical development activities;
- our manufacturing plans, capabilities and strategy;
- our intellectual property position and strategy;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our use of the proceeds from the private placement completed in February 2021;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

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

You should read this Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

REFERENCES TO CATABASIS

Except as otherwise indicated herein or as the context otherwise requires, references in this Annual Report on Form 10-K to "Catabasis," "the Company," "we," "us," and "our" refer to Catabasis Pharmaceuticals, Inc. and its consolidated subsidiaries.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics. Our mission is to bring hope with life-changing therapies to patients and families that are affected by rare diseases. Our lead product candidate is QLS-215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in preclinical development for the treatment of hereditary angioedema, or HAE, a rare, debilitating and potentially life-threatening disease.

In January 2021, as further described below, we acquired Quellis Biosciences, Inc., or Quellis, including the QLS-215 program, and announced a private placement that, upon closing in February 2021, resulted in gross proceeds to us of approximately $110.0 million before deducting placement agent and other offering expenses. In November 2020, after we stopped the development of our edasalonexent program as a potential treatment for Duchenne Muscular Dystrophy, or DMD, we decided to explore and evaluate strategic options and engaged Ladenburg Thalmann & Co., Inc. as our strategic financial advisor. The acquisition of Quellis was the result of our evaluation of strategic options and we believe that the acquisition represents an opportunity to create substantial value for our stockholders.

HAE is a rare, debilitating and potentially life-threatening disease. The treatment options for patients with HAE have improved, however there is remaining unmet medical need and the global market for HAE therapy is strong and growing. The vision for our lead program, QLS-215, is to develop a best-in-class monoclonal antibody inhibitor of plasma kallikrein for HAE prophylaxis that is able to treat HAE by achieving sustained blood levels of QLS-215 with infrequent dosing. Plasma kallikrein is a critical component of HAE that causes pathologic vascular permeability, vasodilation and ultimately excessive tissue swelling. QLS-215 is a humanized monoclonal antibody targeting plasma kallikrein that has shown in preclinical studies that it may potentially enable patients to dose less frequently and potentially be more effective than existing HAE treatments. QLS-215 is currently in preclinical development and we expect to submit an Investigational New Drug application, or IND, for QLS-215 in the first half of 2022 and plan to initiate a Phase 1a clinical trial with initial results anticipated by the end of 2022. Subsequently, assuming positive data from the Phase 1a clinical trial, we plan to initiate a Phase 1b/2 trial in patients with HAE in 2023 with initial results anticipated by the end of 2023. We believe that these clinical trials have the opportunity to establish proof of concept for the differentiated profile of QLS-215.

Previously, our lead program was edasalonexent, which was in Phase 3 clinical development for the treatment of DMD. In October 2020, we announced that the Phase 3 PolarisDMD trial of edasalonexent did not meet its primary endpoint, which was a change from baseline in the North Star Ambulatory Assessment over one year of treatment with edasalonexent compared to placebo. In addition, we announced that the secondary endpoint timed function tests (time to stand, 10-meter walk/run and 4-stair climb) did not show statistically significant improvements. Based on these results, we stopped activities related to the development of edasalonexent, including the GalaxyDMD open-label extension trial. The Phase 3 Polaris DMD trial was a one-year placebo-controlled trial designed to evaluate the safety and efficacy of edasalonexent in boys ages 4-7 (up to 8th birthday) with DMD. The trial enrolled 131 boys across eight countries, with any mutation type, who were not on steroids. Edasalonexent was well-tolerated, consistent with the safety profile seen to date. The majority of adverse events were mild in nature and the most common treatment-related adverse events were diarrhea, vomiting, abdominal pain and rash. There were no treatment-related serious adverse events and no dose reductions. Data from the Phase 3 PolarisDMD trial will be further analyzed and we expect to publish these data.

January 2021 Quellis Acquisition and February 2021 Financing

In January 2021, we acquired Quellis pursuant to an Agreement and Plan of Merger, or the Merger Agreement, by and among us, Cabo Merger Sub I, Inc., a Delaware corporation and our wholly owned subsidiary, or the First Merger Sub, Cabo Merger Sub II, LLC, a Delaware limited liability company and our wholly owned subsidiary, or the Second Merger Sub, and Quellis. Pursuant to the Merger Agreement, the First Merger Sub merged with and into Quellis, pursuant to which Quellis was the surviving entity and

became a wholly owned subsidiary of Catabasis, or the First Merger. Immediately following the First Merger, Quellis merged with and into the Second Merger Sub, pursuant to which the Second Merger Sub was the surviving entity, or the Second Merger and, together with the First Merger, the Merger. Under the terms of the Merger Agreement, at the closing of the Merger, we issued to the Quellis stockholders 3,332,669 shares of our common stock, and 50,504 shares of newly designated Series X Preferred Stock (as described below). In addition, we assumed outstanding Quellis stock options, which became options for our common stock, and assumed a warrant exercisable for Quellis common stock, which became a warrant to purchase 2,805 shares of Series X Preferred Stock at an exercise price of $341.70 per share, and a warrant to purchase 185,136 shares of our common stock at an exercise price of $0.35 per share.

In January 2021, we also entered into a Stock Purchase Agreement, or the Purchase Agreement, with certain institutional and accredited investors, or the Investors, pursuant to which, we sold an aggregate of 35,573 shares of Series X Preferred Stock for an aggregate purchase price of $110.0 million, or the February 2021 Financing. Subject to stockholder approval, each share of Series X Preferred Stock issued in the Merger and pursuant to the Purchase Agreement is convertible into 1,000 shares of common stock. Pursuant to the Merger Agreement, we have agreed to hold a stockholders' meeting to submit the following matters to our stockholders for their consideration: (i) the approval of the conversion of the Series X Preferred Stock into shares of common stock in accordance with Nasdaq Listing Rule 5635(a), or the Conversion Proposal and (ii) if necessary or appropriate, the approval of an amendment to our certificate of incorporation to authorize sufficient shares of common stock after the conversion of the Series X Preferred Stock issued pursuant to the Merger Agreement and the Purchase Agreement and/or to effectuate a reverse stock split, or the Charter Amendment Proposal. Assuming stockholder approval of the Conversion Proposal, on the fourth business day after such approval, each share of Series X Preferred Stock then outstanding would automatically convert into 1,000 shares of common stock, subject to certain beneficial ownership limitations, including that a holder of Series X Preferred Stock is prohibited from converting shares of Series X Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (to be initially set at 9.99% and thereafter adjustable by the holder to a number between 4.99% and 19.99%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion. Shares of Series X Preferred Stock not converted automatically are thereafter subject to conversion at the option of the holder.

Our Product Candidate

QLS-215

QLS-215 is a monoclonal antibody that was designed to inhibit plasma kallikrein for the treatment of HAE. Plasma kallikrein is a critical component of the plasma contact system, which causes pathologic vascular permeability in Type I and Type II HAE. QLS-215 is a humanized monoclonal antibody that was developed through a hybridoma screening and antibody optimization process. Following humanization and optimization for affinity and overall properties, the antibody was modified to increase its plasma half-life. This process resulted in QLS-215, a humanized monoclonal antibody having the following desirable features: high affinity and kallikrein inhibitory activity, selectivity for plasma kallikrein compared to pre-kallikrein, reduced CMC liabilities and extended plasma half-life. Based on these characteristics and preclinical experiments with QLS-215, including in vitro potency results and extended plasma half-life in non-human primates, we believe that QLS-215 has the potential to be a best-in-class monoclonal antibody inhibitor of plasma kallikrein that could combine the benefits of infrequent dosing with the inhibition of edema attacks over long periods of time. We believe that we can establish clinical proof of concept early in the development program with a Phase 1a clinical trial in normal healthy volunteers and a Phase 1b/2 trial in patients with HAE. If we achieve these goals, we believe that we can develop a differentiated, best-in-class new therapy for HAE prophylaxis with a well understood monoclonal antibody modality to provide patients with improved outcomes and quality of life.

Overview of HAE

HAE is a rare, autosomal dominant genetic disorder. The disease is characterized by recurrent, unpredictable, debilitating and potentially life-threatening edema in the skin, abdomen and airway. The vast

majority of HAE cases (Type I and Type II) are caused by defects in the C1 esterase inhibitor gene. Deficiencies in the C1 esterase inhibitor gene result in overproduction of bradykinin, a key mediator of vasodilation and angioedema. In several other types of HAE, which are a small minority of cases, other mutations (e.g., in the Factor XII gene) can cause HAE. The estimated prevalence of Type I and Type II HAE range from 1 in 10,000 to 1 in 50,000 with fewer than an estimated 8,000 patients in the United States and fewer than an estimated 15,000 patients in Europe with HAE. There are active and knowledgeable HAE patient advocacy organizations in the United States and internationally.

Patients with HAE are typically diagnosed by the age of 20 with the average age of disease onset around 11. The severity and frequency of swelling attacks is highly variable even between family members.

The Role of Plasma Kallikrein in Hereditary Angioedema

Plasma kallikrein is an enzyme that cleaves high molecular weight kininogen, or HMWK, to release bradykinin. Normally, circulating C1 esterase inhibitor (C1INH) limits the activation of plasma kallikrein from its precursor prekallikrein, and thereby prevents the release of excess bradykinin from the cleavage of HMWK by plasma kallikrein. In HAE associated with C1INH deficiency, plasma kallikrein is hyperactive, resulting in excessive bradykinin release. Bradykinin activates the bradykinin receptor (B2R) in endothelial cells, resulting in increased vascular permeability and release of fluid into subcutaneous tissue spaces, or angioedema. Thus, unchecked plasma kallikrein activity is a critical component that causes pathologic vascular permeability and vasodilation in HAE, leading to excessive tissue swelling, a primary clinical symptom.

Unaddressed Market Opportunity

There are two treatment approaches to managing the unpredictable and recurrent edema attacks typically experienced by people with HAE. On-demand treatments are administered at the onset of an attack to reduce the severity and duration of the attack, and prophylactic, or preventative, treatments are taken chronically to reduce the frequency and severity of future attacks. In the United States, the Food and Drug Administration, or FDA, has approved four therapies for on-demand treatment of HAE: BERINERT® (C1 esterase inhibitor [human]), FIRAZYR® (icatibant injection), KALBITOR® (ecallantide) and RUCONEST® (C1 esterase inhibitor [recombinant]). For long-term prophylactic treatment of HAE, the FDA has approved the following four therapies: CINRYZE® (C1 esterase inhibitor [human]), HAEGARDA® (C1 esterase inhibitor subcutaneous [human]), TAKHZYRO® (lanadelumab-flyo) and ORLADEYO™ (berotralstat). With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States. The approved prophylactic therapies have provided HAE patients with treatment options but have limitations in dosing frequency, side effects and/or efficacy. CINRYZE and HAEGARDA are administered twice a week; CINRYZE by intravenous, or IV, infusion and HAEGARDA by subcutaneous, or SC, injection. TAKHZYRO is dosed twice a month by SC injection. Dosing every four weeks may be considered in some patients. With these injectable therapies, patients have reported a desire for less burdensome administration. ORLADEYO is an oral capsule taken daily with food, and data from its approved label, while not comparative data, suggest a lower percentage reduction in attack rate than other available therapies. Historically, androgens and antifibrinolytic treatments have also been used to treat HAE prophylactically but they are associated with side effects such as hypertension, acne, hirsutism, rashes, amenorrhea, liver enzyme elevations and increased risk of thrombosis and their overall use has been declining with the ability of more-tolerable, HAE-specific therapies. Although there has been progress with recent innovation in therapies for HAE and, as described in the section entitled "Competition" in this Business section, there are a significant number of product candidates in HAE for clinical and pre-clinical development, we believe that there is remaining unmet medical need for potent and long duration of action prophylactic therapies to provide patients with lower burden of treatment and improved outcomes and quality of life.

Preclinical Results

A physiologically relevant functional assay was used to characterize the *in vitro* potency of QLS-215 as compared to lanadelumab, another monoclonal antibody known to inhibit plasma kallikrein. Lanadelumab is commercialized under the brand name TAKHZYRO and approved as a prophylactic treatment for

HAE. The assay measured bradykinin release from HMWK as catalyzed by plasma kallikrein. The assay parameters were physiologically relevant due to the concentration of HMWK being the concentration that circulates in humans and the concentration of plasma kallikrein being in the range of what has been estimated in plasma from patients with HAE during an attack. Both QLS-215 and lanadelumab showed a dose-dependent inhibition of bradykinin, indicating reduced plasma kallikrein activity and QLS-215 exhibited a greater potency for inhibition of plasma kallikrein activity and bradykinin release than lanadelumab, as shown in the figure below.

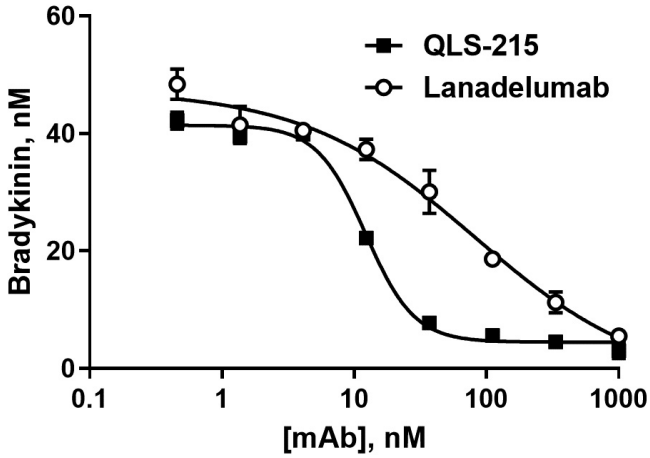

Figure 1 — Functional Assay for Plasma Kallikrein Inhibition

In HAE, the therapeutically relevant level of inhibition to prevent HAE attacks is thought to be approximately 90% inhibition of plasma kallikrein. This corresponds to a measurement referred to as IC90, which is the concentration of an agent that results in a 90% inhibitory effect. In the functional assay shown in the figure above, the IC90 for QLS-215 was approximately 30 nM and the IC90 for lanadelumab was approximately 300 nM, indicating that QLS-215 had approximately 10-fold higher potency than lanadelumab. The results of this assay are consistent with what has been observed for clinical efficacy for lanadelumab, as clinical trials with lanadelumab have shown that steady state plasma levels of lanadelumab of 200-300 nM are required to optimally reduce the HAE attack rate and maximize attack-free duration.

In separate studies, cynomolgus monkeys were used to evaluate the pharmacokinetics and plasma half-life of QLS-215 as well as lanadelumab. These studies of QLS-215 and lanadelumab were conducted concurrently but were independent studies rather than a head-to-head comparison. In these studies, lanadelumab was observed to have a half-life of approximately 10 days, which is consistent with what has been reported in FDA review documents and publications for lanadelumab in non-human primates. This half-life is also consistent with what has been reported for similar antibodies. QLS-215 was administered at the same dose as lanadelumab in these studies and the observed half-life of QLS-215 was approximately 34 days, which is about a 3 to 4-fold longer half-life than observed for lanadelumab, as shown in the figure below. We believe this could translate to a half-life of several months for QLS-215 in humans. If this longer half-life is demonstrated in clinical trials, it has the potential to enable infrequent dosing.

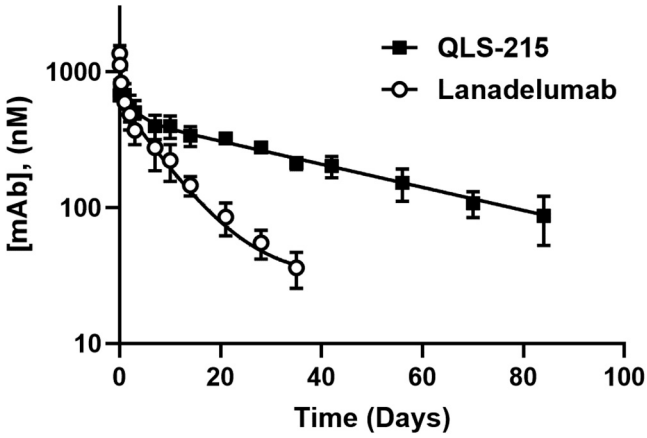

Figure 2 — Pharmacokinetics in cynomolgus monkeys for QLS-215 and lanadelumab. Data from concurrent but independent experiments in cynomolgus monkeys. Lanadelumab data are representative of three independent experiments that all showed a half-life of approximately 10 days.

Taken together, the half-life results from the cynomolgus monkey studies and the data from the *in vitro* potency assay can be interpreted to suggest a potential duration of efficacy for the antibodies. Specifically, the measured plasma concentration of an antibody at each timepoint from the cynomolgus monkey studies can be used to predict an expected level of plasma kallikrein inhibition at that time point based on the plasma kallikrein inhibition observed for that concentration of antibody in the *in vitro* potency assay. In the cynomolgus monkey studies, lanadelumab plasma levels fell below the minimum therapeutic concentration, or IC90, predicted by the *in vitro* potency assay by approximately day 10, and by day 20 were at levels the *in vitro* potency assay predicted would result in approximately 50% inhibition of plasma kallikrein. In contrast, in the cynomolgus monkey studies, QLS-215 plasma levels remained above the IC90 predicted by the *in vitro* potency assay for 84 days, which was the full duration of the experiment. These preclinical data suggest that at equal doses QLS-215 would have a significantly longer duration of action than lanadelumab. This could potentially enable a lower dose of QLS-215 that would have a longer duration of action than lanadelumab. We believe that this could result in QLS-215 being an effective prophylactic therapy for patients with HAE due to inhibition of the pathological activity of plasma kallikrein for an extended time period.

Preclinical and Clinical Development Plans

We plan to conduct IND-enabling activities and initiate cGMP manufacturing of QLS-215 in 2021. We have commenced cell line development with a contract manufacturer and high producing proprietary cell lines have been identified that we believe will be sufficient to generate material for toxicology studies and the master cell bank. We plan to submit an IND for QLS-215 in the first half of 2022 and plan to initiate the Phase 1a clinical trial with initial results anticipated by the end of 2022. Subsequently, assuming positive data from the Phase 1a clinical trial, we plan to initiate a Phase 1b/2 trial in patients with HAE in 2023 with initial results anticipated by the end of 2023. We believe that these clinical trials have the opportunity to establish proof of concept for the differentiated profile of QLS-215.

Our objective for our planned early clinical trials is to establish clinical proof of concept to support the profile that we anticipate for QLS-215 in terms of activity and half-life. We expect the Phase 1a clinical trial to be conducted in healthy volunteers with single escalating doses. The primary goals for the Phase 1a trial would be to demonstrate safety and extended half-life as proof of concept in humans and to explore pharmacodynamic activity of QLS-215 utilizing ex vivo functional assays. We also expect that results from the Phase 1a trial, if favorable, have the potential to allow us to plan and initiate our planned Phase 1b/2 clinical trial in patients with HAE. The primary goals for this second trial would be to demonstrate safety and extended half-life as proof of concept in patients with HAE and to determine plasma kallikrein inhibitor activity of QLS-215 with pharmacodynamic assessments. We see this as an opportunity to demonstrate clinical proof of concept in patients with HAE and to monitor HAE attacks as an exploratory assessment.

Competition

The development and commercialization of new drugs is highly competitive. If we successfully develop and commercialize QLS-215, we and any future collaborators will face competition from pharmaceutical and biotechnology companies worldwide. Many of the entities developing and marketing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing. Even if we are able to successfully develop and commercialize QLS-215, our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than QLS-215.

The key competitive factors affecting the success of QLS-215, if approved, are likely to be its efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

In the United States, the FDA has approved four therapies for on-demand treatment of HAE: BERINERT, FIRAZYR, KALBITOR and RUCONEST. For long-term prophylactic treatment of HAE, the FDA has also approved four therapies: CINRYZE, HAEGARDA, TAKHZYRO and ORLADEYO. There are four main manufacturers of therapies for HAE, CSL Behring (BERINERT and HAEGARDA), Takeda (FIRAZYR, KALBITOR, CINRYZE and TAKHZYRO), Pharming (RUCONEST) and BioCryst (ORLADEYO). With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States. Historically, androgens and antifibrinolytic treatments have also been used prophylactically to treat HAE, however their use is declining with the availability of more-tolerable, HAE-specific therapies.

On-demand and prophylactic HAE therapies target one of three primary mechanisms. CSL Behring's BERINERT and HAEGARDA, Pharming's RUCONEST and Takeda's CINRYZE are C1 inhibitor replacement therapies. Takeda's FIRAZYR is a Bradykinin 2 receptor antagonist, and Takeda's KALBITOR, TAKHZYRO and BioCryst's ORLADEYO target plasma kallikrein. TAKHZYRO is a monoclonal antibody and KALBITOR and ORLADEYO are small molecule inhibitors.

On-demand therapies are taken as needed; BERINERT and RUCONEST are IV infusions approved for adult and pediatric patients, FIRAZYR is a SC injection, approved for adults 18 and older, and KALBITOR is a series of 3 SC injections, approved for patients 12 years and older. KALBITOR must be administered by a healthcare professional to monitor for the risk of anaphylactic reactions.

Prophylactic therapies are taken chronically. CINRYZE is an IV infusion and HAEGARDA is an SC injection; both are administered twice a week and are approved for adult and pediatric patients 6 years and older. TAKHZYRO is an SC injection generally administered every two weeks; however dosing every four weeks may be considered in some patients. TAKHZYRO is approved for patients 12 years and older. ORLADEYO is an oral capsule taken once daily with food for patients 12 years and older. Given that TAKHZYRO is an approved monoclonal antibody inhibitor of plasma kallikrein, if QLS-215 is approved, we expect that it will compete most directly with TAKHZYRO.

We are aware of additional programs in development for HAE, which are focused largely on prophylactic approaches. For example, CSL Behring CSL312's (garadacimab) is a novel investigational factor XIIa-inhibitory monoclonal antibody (FXIIa mAb) that is in Phase 3 development for HAE prophylaxis. KalVista Pharmaceuticals is developing two small molecule plasma kallikrein inhibitors: KVD900, which is in Phase 2 development for on-demand treatment of HAE, and KVD824, which is in Phase 1 development for prophylactic treatment. Ionis Pharmaceuticals is developing IONIS-PKK-LRx, which is an antisense inhibitor of prekallikrein synthesis that is in Phase 2 development, and Attune Pharmaceuticals is developing ATN-249, an oral plasma kallikrein inhibitor that is in Phase 1 development for prophylactic treatment. Generium's GNR-038 is a C1 inhibitor that is in Phase 1 development for prophylactic therapy and Pharvaris has completed a Phase 1 program for a B2 receptor antagonist, PHVS121, and has stated that it intends to formulate this compound as an oral capsule for on-demand treatment (PHVS416) and as an extended-release tablet for prophylactic treatment (PHVS719). There are also additional companies that have potential gene therapy and gene editing approaches for HAE in preclinical development that if successful, could impact the need for treatments for HAE, including Biomarin Pharmaceutical (BMN331), Intellia Therapeutics (NTLA-2002) and RegenxBio (unnamed program).

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business. This includes plans to pursue and maintain patent protection intended to cover the composition of matter of QLS-215, its method of use, and other related technologies and inventions that are important to our business. In addition to seeking patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for commercially important technologies, inventions and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

We own one United States provisional patent application directed to our product candidate QLS-215 and its use in treating various disorders including HAE. Any granted patent claiming priority to this provisional application, if issued, would expire in 2042, assuming all maintenance fees are paid.

The patent positions for biopharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that our QLS-215 product candidate will be protected or remain protectable by enforceable patents, even if issued. We cannot predict whether the patent application we are currently pursuing will issue as a granted patent in any particular jurisdiction or whether the claims of any granted patent will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries where we may elect to file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in granting a patent. A United States patent term may be shortened, if a patent is terminally disclaimed by its owner, over another patent.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that an issued United States patent covering QLS-215 may be entitled to a patent term extension. If our QLS-215 product candidate receives FDA approval, we intend to apply for a patent term extension, if available, to extend the term of the patent that covers the approved product candidate. We also intend to seek patent term extensions in any jurisdictions where they are available. However, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we may rely on other forms of regulatory and legislative non-patent exclusivity protection that are typically triggered by marketing approval of a product. In the U.S, these include orphan drug exclusivity, pediatric exclusivity, new chemical entity exclusivity and, for biologics such as QLS-215, reference product exclusivity. The European Union and many other key markets outside the United States have comparable forms of such exclusivity. However, there is no guarantee that we will obtain any of these forms of exclusivity protection for QLS-215 or any future product candidate. We also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors, contract research organizations, and potential

collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

Manufacturing and Supply

We do not own or operate manufacturing facilities. We currently rely on third-party manufacturers and suppliers for the antibodies used to make QLS-215, and we expect to continue to do so to meet our nonclinical, clinical and commercial activities. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our relationships with contract manufacturers. Our third-party manufacturers are required to manufacture QLS-215 and any future product candidates under current Good Manufacturing Practice, or cGMP, requirements and other applicable laws and regulations. We believe there are multiple sources for all the materials required for the manufacture of QLS-215.

As noted above, we have commenced cell line development for QLS-215 with a contract manufacturer and high producing proprietary cell lines have been identified that we believe will be sufficient to generate material for toxicology studies and the master cell bank. We plan to initiate cGMP manufacturing for QLS-215 in 2021. The process of manufacturing biologics such as QLS-215 is complex, highly regulated and subject to multiple risks. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, other supply disruptions and higher costs. If microbial, viral or other contaminations are discovered at the facilities of our third-party contract manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials, result in higher costs of drug product and adversely affect our business.

Human Capital

As of December 31, 2020, we had 20 employees, 10 of whom were primarily engaged in research and development activities. A total of 7 employees have Ph.D. degrees. None of our employees is represented by a labor union and we believe our relations with our employees are good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and to align such awards with the interests of our stockholders.

Sales and Marketing

Given our stage of development, we have not yet determined our commercial strategy or established a formal commercial organization infrastructure or distribution capabilities, nor have we entered into any collaboration or co-promotion arrangements.

Government Regulation and Product Approval

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

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Biological products are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations. An applicant seeking approval to market and distribute a new drug or biological product in the United States must typically secure the following:

- completion of preclinical laboratory tests in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- submission to the FDA of a new drug application, or NDA, for a drug candidate product and a biological licensing application, or BLA, for a biological product requesting marketing for one or more proposed indications;
- review of the request for approval by an FDA advisory committee, where appropriate or if applicable;
- completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMPs to assure the product's identity, strength, quality and purity;
- completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured substance or active pharmaceutical ingredient and the formulated product, as well as in vitro and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer an investigational product candidate to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions

about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

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

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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

The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. 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 DSMB, or committee. This group provides authorization for whether a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made based on evolving business objectives and/or competitive climate.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

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

When considering an IND for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product. Companies are required to make their expanded access policies publicly available upon the earlier of initiation of a phase 2 or phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, sponsors are required to make policies for evaluating and responding to requests for expanded access for patients publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy. In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Studies in Support of an NDA or BLA

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

The clinical investigation of an investigational drug or biological product is generally divided into four phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The four phases of an investigation are as follows:

- ***Phase 1.*** Phase 1 studies include the initial introduction of an investigational new drug or biological product into humans. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- ***Phase 2.*** Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under trial, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population.
- ***Phase 3.*** Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval.

- ***Phase 4.*** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Pediatric Studies

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

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act, or FDASIA. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In 2017, with passage of the FDA Reauthorization Act of 2017, or FDARA, Congress further modified these provisions. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act.

Submission and Review of an NDA or BLA by the FDA

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the proposed drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's CMCs and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product,

or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The application is the vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2021 is $336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses. If an application is withdrawn prior to the FDA acceptance for filing, 75% of these fees may be refunded to the sponsor. If an application is withdrawn after filing, a lower portion of these fees may be refunded in certain circumstances.

Following submission of an NDA or BLA, the FDA conducts a preliminary review of the application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an NDA or BLA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a Complete Response Letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the application, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the application in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of an application if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product. If the FDA

approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions which can materially affect the potential market and profitability of the product. In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is an NME.

The FDA also may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

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

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

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

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to help the sponsor design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this

designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Regulation

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also

are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data

exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Biosimilars

The 2010 Patient Protection and Affordable Care Act, or ACA, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2021, the FDA has approved 29 biosimilar products for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidance is expected to be finalized by FDA in the near term.

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

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

Orphan Drug Designation and Exclusivity

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

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

same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with orphan drug exclusivity is not able to meet market demand or the subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan drug exclusivity regardless of a showing of clinical superiority. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA.

Pediatric Exclusivity

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

Patent Term Restoration and Extension

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

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member

states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application, or CTA, must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will become directly applicable to and binding in all 28 European Union Member States without the need for any national implementing legislation. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting European Union Member State (RMS) through a European Union Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single European Union Member State or in more than one European Union Member State.

The Regulation was published on June 16, 2014 but has not yet become effective. As of January 1, 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

As in the US, parties conducting certain clinical trials must post clinical trial information in the European Union at the EudraCT website.

PRIME Designation in the European Union

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the CHMP or Committee for Advanced Therapies, or CAT, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level.

Pediatric Studies

In the European Economic Area, or EEA, companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's pediatric committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date.

Marketing Authorization

In the EEA, medicinal products can only be commercialized after obtaining a marketing authorization. Marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application, or MAA, is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other concerned European Union Member States of an assessment of an application for marketing authorization conducted by one European Union Member State, known as the reference European Union Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference European Union Member State and the concerned European Union Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference European Union Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned European Union Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned European Union Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all European Union Member States.

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

Regulatory Data Protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies.

Pediatric Exclusivity

Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Orphan Drug Designation and Exclusivity in the European Union

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

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

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

Regulatory Requirements After Marketing Authorization

Following marketing authorization of a medicinal product in the European Union, the holder of the authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the European Union's stringent pharmacovigilance or safety reporting, as well as rules potentially requiring post-authorization studies and additional monitoring obligations. In addition, the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with European Union cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union. Finally, the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/

83EC, as amended, and European Union Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the European Union.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom left the European Union on January 31, 2020, commonly referred to as "Brexit." On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the UK, as the UK legislation now has the potential to diverge from European Union legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like a European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the European Union 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the European Union /EEA remain unaffected.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to GDPR. GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid,

commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

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

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

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019,

the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the United States Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew the DOJ's support for this lawsuit. A ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent United States congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow

companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

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

Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid; the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-United States officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Our Corporate Information

Our executive offices are located at 100 High Street, 28th Floor, Boston, Massachusetts, 02110, and our telephone number is (617) 349-1971. Our website address is www.catabasis.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website located at www.catabasis.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission, or the SEC. These reports are also available at the SEC's Internet website at www.sec.gov. Our website and the information contained therein or connected thereto are not intended to be incorporated into this Annual Report on Form 10-K.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.catabasis.com, under "Investors — Corporate Governance".

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing business environment that involves risks and substantial uncertainty. The following discussion addresses risks and uncertainties that could cause, or contribute to causing, actual results to differ from expectations in material ways. In evaluating our business, investors should pay particular attention to the risks and uncertainties described below and in other sections of this Annual Report on Form 10-K and in our subsequent filings with the SEC. These risks and uncertainties, or other events that we do not currently anticipate or that we currently deem immaterial also may affect our results of operations, cash flows and financial condition. The trading price of our common stock could also decline due to any of these risks, and you could lose all or part of your investment.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our business is almost entirely dependent on the success of QLS-215 as a potential treatment for HAE, a program that we only recent acquired and that is in pre-clinical development.

Our business is almost entirely dependent on the success of QLS-215, which is in the pre-clinical stage of development, and has only produced results in pre-clinical and non-clinical settings. We acquired QLS-215 in connection with our acquisition of Quellis in January 2021. The acquisition of Quellis involves numerous risks, including the inability to effectively integrate the QLS-215 program into our preclinical and clinical operations or realize the expected benefits from the acquisition, which could materially harm our operating results. We cannot give any assurance that we will generate clinical or other data for QLS-215 sufficiently supportive to receive regulatory approval, which will be required before it can be commercialized. We have not filed an IND with the FDA for QLS-215 and have had no interactions with the FDA regarding our clinical development plans for QLS-215. We may experience issues surrounding preliminary trial execution, such as delays in filing our planned IND, delays in FDA acceptance of our planned IND, revisions in trial design and finalization of trial protocols, difficulties with patient recruitment and enrollment, quality and provision of clinical supplies, or early safety signals. QLS-215 will require significant preclinical and clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales.

Until late 2020, we were largely focused on discovering and developing novel small molecule drugs by applying our SMART Linker drug discovery platform. With the acquisition of Quellis, we have shifted our focus to QLS-215. Unlike our prior product candidates, which were small molecules, QLS-215 is a humanized monoclonal antibody. As a result, we will face different regulatory, manufacturing, and research and discovery requirements and demands.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of QLS-215, which may never occur. Given that QLS-215 is in preclinical development, it will be years before we are able to demonstrate safety and efficacy of QLS-215 sufficient to warrant approval for commercialization, and we may never be able to do so. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize QLS-215, we may not be able to generate sufficient revenue to continue our business and our business would be materially harmed.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies, including us, in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in preclinical studies or early development, and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

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, 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 receive positive results in preclinical studies or clinical trials of QLS-215 or any other future product candidate, the development timeline and regulatory approval and commercialization prospects for such product candidate, and, correspondingly, our business and financial prospects would be negatively impacted.

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

We have limited financial and managerial resources and have expended significant resources on the development of our edasalonexent program, which has proven to be unsuccessful. We are now shifting our focus to the preclinical and clinical development of QLS-215 as a potential treatment for HAE, a rare disease with unmet medical need, and we would expect that development of any other future product candidate would also be for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials and we may be unsuccessful in identifying any new product candidates.

Our lead product candidate, QLS-215, is still in the preclinical stage, and its risk of failure is high. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States, or similar applications in other jurisdictions. Such studies are complex and may be subject to delays or increased costs due to our dependence upon third parties to assist us with such studies and the ability to source raw materials and the appropriate animals, including non-human primates, so that we can conduct such testing. In the event that the FDA or comparable foreign regulatory authorities require us to complete additional preclinical studies or we are required to satisfy other FDA requests or other requests of comparable foreign regulatory authorities prior to commencing clinical trials, the start of our planned clinical trials may be delayed. Even after we receive

and incorporate guidance from the FDA or comparable foreign regulatory authorities, such authorities may not agree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or comparable foreign regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or comparable foreign regulatory authorities allowing clinical trials to begin.

In addition, any future research programs to identify new product candidates will require substantial technical, financial and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome. If clinical trials of a product candidate fail to satisfactorily demonstrate safety and efficacy to the FDA and other comparable foreign regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining approval from the FDA of a Biologics License Application, or BLA, which would be required for approval of QLS-215, or New Drug Application, or NDA. Comparable foreign regulatory authorities, such as the European Medicines Agency, or the EMA, require similar approvals. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy in humans of any product candidate that we may choose to develop before we, or they, will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials we initiate will be conducted as planned or completed on schedule, or at all. Further, the clinical development of product candidates is susceptible to the risk of failure at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if a product candidate that we choose to develop has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in any clinical trials we conduct, we may fail to detect toxicity of or intolerability caused by a product candidate, or mistakenly believe that a product candidate is toxic or not well tolerated when that is not in fact the case.

We have not previously submitted an NDA or BLA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. Moreover, our prior programs were not biologics and this lack of experience may impede our ability to successfully complete clinical development of QLS-215 or any future biologic product candidates we pursue and obtain FDA approval in a timely manner, if at all. Any inability to complete clinical development successfully could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any future collaborators, are required to modify our trial designs, such as required modifications with respect to

patient populations, endpoints, comparators or trial duration, (2) we, or any future collaborators, are required to conduct additional clinical trials or other testing of a product candidate beyond the trials and testing that we, or they contemplate, (3) we, or any future collaborators, are unable to successfully complete clinical trials of a product candidate or other testing, (4) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (5) there are unacceptable safety concerns associated with a product candidate, we, or any future collaborators, may:

- be delayed in obtaining marketing approval for such product candidate;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements, such as a REMS program; or
- be required to remove the product from the market after obtaining marketing approval.

Given our early stage of development, it will be years before we are able to demonstrate the safety and efficacy of a treatment sufficient to warrant approval for commercialization, and we may never be able to do so. Our failure to successfully complete clinical trials of a product candidate and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of a product candidate would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any of any future product candidate may be identified during development that could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any future product candidate could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of such product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any such product candidate is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of any future product candidate, potential marketing approval or commercialization of such product candidate could be delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval or commercialization of any future product candidate, including:

- clinical trials may produce unfavorable or inconclusive results;
- we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials may be larger than we, or any future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;
- the cost of planned clinical trials may be greater than we anticipate;

- our third-party contractors or those of any future collaborators, including those manufacturing such product candidate or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any future collaborators in a timely manner or at all;
- regulators or institutional review boards may not authorize us, any future collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any future collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any future collaborators, may have to delay, suspend or terminate clinical trials for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, or travel bans or other restrictions imposed by applicable governmental authorities due to the ongoing COVID-19 pandemic;
- regulators or institutional review boards may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any future collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any future collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply, due to, among other things, the ongoing COVID-19 pandemic; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

In addition, we may conduct clinical trials outside of the United States. Unforeseen global instability, including political instability, or instability from an outbreak of pandemic or contagious disease, such as the ongoing COVID-19 pandemic, in or around any countries in which we conduct clinical trials, could affect our ability to enroll patients in clinical trials in these countries, prevent patients already enrolled from completing such clinical trials, and/or cause other trial delays or otherwise adversely impact such clinical trials.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of any future product candidate. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize product candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do and impair our ability, or the ability of any future collaborators, to successfully commercialize product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any future product candidates.

If we, or any future collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.

We, or any future collaborators, may not be able to initiate or continue clinical trials for QLS-215 or any other future product candidate if we, or they, are unable to locate and enroll, and maintain the enrollment of, a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any existing or newly approved drugs that may be approved for the indications we are investigating.

Our ability to successfully complete any future clinical trial for QLS-215 as a potential treatment for HAE or for any other future product candidate for the treatment of any rare disease or any other indication will be dependent upon our ability to enroll, and maintain the enrollment of, a sufficient number of patients with such disease, which will be subject to a number of risks and uncertainties. For example, rare diseases, including HAE, have small patient populations and often have only a limited number of specialist physicians that regularly treat such patients. Further, these specialized sites typically treat a range of diseases and, at any point in time, may have constrained resources and capacity to handle clinical trials. In addition, in the case of HAE, the indication on which we are currently focused, approved products are available for the rare disease and therefore patients and their healthcare providers may feel satisfied with their treatments and therefore not feel the need to participate in a clinical trial for another product candidate for the same disease or the criteria for the trial may not allow patients on such other therapies to enroll in the trial. Additionally, in the case of HAE, diagnosis is often delayed from onset of symptoms and patients that might be eligible for enrollment in our trials may not have been diagnosed and therefore are unaware of such eligibility. Finally, other companies may be conducting clinical trials or may have announced plans for future clinical trials that are seeking, or are likely to seek, to enroll patients with the disease and patients are generally only able to enroll in a single trial at a time. The small population of patients, competition for these patients and the limited trial sites and their constrained resources may make it difficult for us to enroll enough patients, and to maintain the enrollment of enough patients, to complete clinical trials for any such future product candidate.

The clinical trials that we may conduct may also have inclusion criteria that further limit the population of patients that we are able to enroll. These inclusion criteria could further limit the available patient pool and present challenges to clinical trial enrollment.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for any clinical trials, including potential clinical trials for QLS-215 as a treatment for HAE, that we or they may determine to pursue could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in any such clinical trials may result in increased development costs for the applicable product candidates, delay or halt the development of and approval processes for any future product candidates and jeopardize our, or any future collaborators', ability to commence sales of and generate revenues from any future product candidates, which could cause the value of our company to decline.

Business disruptions could delay completion of future clinical trials, seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of third-party research institution collaborators, contract research organizations, contract manufacturing operations, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics such as the ongoing COVID-19 pandemic, and other natural or man-made disasters or business interruptions, for which we may be partly uninsured. In addition, to the extent we determine to pursue development of future product candidates, we expect that we will rely on third-party research institution collaborators for conducting research and development of such product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could delay completion of any clinical trials for such product candidates, seriously harm our operations and financial condition and increase our costs and expenses.

The COVID-19 pandemic has had, and continues to have, significant impacts worldwide, and may delay the initiation of future clinical trials, disrupt or increase the costs of regulatory or manufacturing activities, or have other adverse effects on our business and operations. In addition, this ongoing pandemic has adversely impacted economies worldwide and may disrupt the financial markets, both of which could result in adverse effects on our business and operations and ability to raise capital.

The COVID-19 pandemic has had, and continues to have, significant impacts worldwide causing many governments to implement measures to slow the spread of the outbreak through quarantines, travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response, including widespread emergency orders requiring business and residents to curtail non-essential activities, have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The development of QLS-215 or any other future product candidates could be negatively impacted by the COVID-19 pandemic for a variety of reasons, including delays of the initiation, recruitment and overall timing of clinical trials, the disruption or delays of regulatory or manufacturing activities, including due to facility shut downs, capacity constraints at third party manufacturers due to the focus on vaccines and other treatments for COVID-19, and increased costs or the inability to source key raw materials that are being diverted for COVID-19 efforts, or other adverse effects that negatively impact our business or operations. The future progression and unpredictability of the pandemic and its effects on our business and operations are highly uncertain and will depend on future developments that cannot be predicted with confidence, such as the widespread use and distribution of the vaccines, the ultimate geographic spread of the disease, the duration of the outbreak, additional surges in the number of cases or deaths from COVID-19, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The pandemic also caused an initial significant disruption in the financial markets, and may cause future such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will continue to significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations, and prospects.

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

We have never obtained marketing approval for a product candidate. We have not yet succeeded and may never succeed in demonstrating efficacy and safety for any of our product candidates in a Phase 3 clinical trial or in obtaining marketing approval thereafter. For example, although we have discovered and evaluated numerous compounds using our SMART Linker drug discovery platform, no product created using the SMART Linker drug discovery platform has ever been approved for sale.

If we are able to advance QLS-215 or any other future product candidate into late-stage development, it is possible that the FDA, EMA or other applicable regulatory authority may refuse to accept for substantive review any applications that we submit for marketing approval of such product candidates or may conclude after review of our data that our applications are insufficient to obtain marketing approval of such product candidate. If the FDA, EMA or other applicable regulatory authority does not accept or approve any applications that we submit for marketing approval, they may require that we conduct additional clinical or nonclinical studies, or conduct manufacturing validation studies, and submit that data before they will reconsider our applications. Depending on the extent of these or any other required studies, approval of any application that we submit may be delayed by several years or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA, EMA or other applicable regulatory authority.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing QLS-215 or any future product candidate, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for any future product candidates, which could significantly harm our business.

If any future product candidate receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.

Clinical trials of product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that clinical trials for QLS-215 and any other future product candidate, or those of any future collaborator, may indicate an apparent positive effect of such product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- we may become the subject of government investigations, which would be expensive to manage and potentially result in the imposition of fines, injunctions or the imposition of civil or criminal penalties;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

Even if a product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for the product candidate may be smaller than we estimate.

Even if QLS-215 or any future product candidate of ours is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians,

patients, third-party payors and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of future product candidates may require significant resources and may not be successful. If QLS-215 or any other future product candidate of ours is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of QLS-215 or any other future product candidates of ours, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to existing approved treatments or alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy and whether there is an existing standard of care;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing, market access and distribution support;
- the approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products;
- availability and amount of reimbursement from government payors, managed care plans and other third-party payors;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

The potential market opportunities for product candidates are difficult to estimate precisely. Any estimates we make as to the potential market opportunities for QLS-215 or any future product candidates will be predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. These assumptions will involve the exercise of significant judgment on the part of our management, will be inherently uncertain and the reasonableness of these assumptions may not have been assessed by an independent source. If any such assumptions prove to be inaccurate, the actual markets for any such future product candidate could be smaller than our estimates of the potential market opportunities.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any future product candidates that we may develop if and when those product candidates are approved.

We currently do not have a formal sales, marketing or distribution infrastructure. To achieve commercial success for any approved product, we would need to either develop a sales and marketing organization or

outsource these functions to third parties. We expect to use a combination of focused in-house sales and marketing capabilities and third-party collaboration, licensing and distribution arrangements to sell any products that receive marketing approval.

We generally expect that we would seek to retain full commercialization rights for products that we can commercialize with a specialized sales force and to retain co-promotion or similar rights when feasible in indications requiring a larger commercial infrastructure. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, at such time as we need to, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to a product, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

We may collaborate with third parties for commercialization of any products that require a large sales, marketing and product distribution infrastructure. We intend to potentially commercialize product candidates through collaboration, licensing and distribution arrangements with third parties. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidates that receive marketing approval.

We face substantial competition from other pharmaceutical and biotechnology companies, and our operating results may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We expect that we, and any future collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any product candidates that we, or they, may seek to develop or commercialize in the future.

We are developing QLS-215 for the treatment of HAE. In the United States, the FDA has approved four therapies for on-demand treatment of HAE: BERINERT, FIRAZYR, KALBITOR, and RUCONEST. For long-term prophylactic treatment of HAE, the FDA has also approved four therapies: CINRYZE, HAEGARDA, TAKHZYRO, and ORLADEYO. There are 4 main manufacturers of therapies for HAE, CSL Behring (BERINERT and HAEGARDA), Takeda (FIRAZYR, KALBITOR, CINRYZE and TAKHZYRO), Pharming (RUCONEST), and BioCryst (ORLADEYO). With the exception of KALBITOR, these therapies are also approved and commercially available outside of the United States. Historically, androgens and antifibrinolytic treatments have also been used prophylactically to treat HAE, however their use is declining with the availability of more-tolerable, HAE-specific therapies.

On-demand and prophylactic HAE therapies target one of three primary mechanisms. CSL Behring's BERINERT and HAEGARDA, Pharming's RUCONEST, and Takeda's CINRYZE are C1 inhibitor replacement therapies. Takeda's FIRAZYR is a Bradykinin 2 receptor antagonist, and Takeda's KALBITOR, TAKHZYRO, and BioCryst's ORLADEYO target plasma kallikrein. TAKHZYRO is a monoclonal antibody and KALBITOR and ORLADEYO are small molecule inhibitors.

On-demand therapies are taken as needed; BERINERT and RUCONEST are IV infusions approved for adult and pediatric patients, FIRAZYR is a SC injection, approved for adults 18 and older, and

KALBITOR is a series of 3 SC injections, approved for patients 12 years and older. KALBITOR must be administered by a healthcare professional to monitor for the risk of anaphylactic reactions.

Prophylactic therapies are taken chronically. CINRYZE is an IV infusion and HAEGARDA is an SC injection; both are administered twice a week and are approved for adult and pediatric patients 6 years and older. TAKHZYRO is an SC injection generally administered every two weeks; however dosing every four weeks may be considered in some patients. TAKHZYRO is approved for patients 12 years and older. ORLADEYO is an oral capsule taken once daily with food for patients 12 years and older. Given that TAKHZYRO is an approved monoclonal antibody inhibitor of plasma kallikrein, if QLS-215 is approved, we expect that it will compete most directly with TAKHZYRO.

We are aware of additional programs in development for HAE, which are focused largely on prophylactic approaches. For example, CSL Behring CSL312's (garadacimab) is a novel investigational factor XIIa-inhibitory monoclonal antibody (FXIIa mAb) that is in Phase 3 development for HAE prophylaxis. KalVista Pharmaceuticals is developing two small molecule plasma kallikrein inhibitors: KVD900, which is in Phase 2 development for on-demand treatment of HAE, and KVD824, which is in Phase 1 development for prophylactic treatment. Ionis Pharmaceuticals is developing IONIS-PKK-LRx, which is an antisense inhibitor of prekallikrein synthesis that is in Phase 2 development, and Attune Pharmaceuticals is developing ATN-249, an oral plasma kallikrein inhibitor that is in Phase 1 development for prophylactic treatment. Generium's GNR-038 is a C1 inhibitor that is in Phase 1 development for prophylactic therapy and Pharvaris has completed a Phase 1 program for a B2 receptor antagonist, PHVS121, and has stated that it intends to formulate this compound as an oral capsule for on-demand treatment (PHVS416) and as an extended-release tablet for prophylactic treatment (PHVS719). There are also additional companies that have potential gene therapy and gene editing approaches for HAE in preclinical development that if successful, could impact the need for treatments for HAE, including Biomarin Pharmaceutical (BMN331) and RegenxBio (unnamed program).

Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable side effects or are less costly than any product candidates that we may develop, which could render any future product candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Our potential future competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

QLS-215 and any other future biologic product candidates will be regulated as biological products, or biologics, and therefore they may be subject to competition from biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product. Under the BPCIA, a reference biological product is granted 12 years of non-patent exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable

product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the other company's product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that QLS-215 and any of our future product candidates, if approved as a biologic product under a BLA, should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If competitors are able to obtain regulatory approval for biosimilars referencing our product candidates, our product candidates may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

If the FDA or comparable foreign regulatory authorities approve generic versions of any future products that receive marketing approval through the NDA pathway, or such authorities do not grant such products appropriate periods of data exclusivity before approving generic versions of our products, our sales could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. We do not know if the FDA will treat the active ingredients in any future product candidates of ours as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that any such products of ours may face from generic versions of such products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability claims as a result of the clinical testing of product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may or they may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical 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, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any future product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

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

Although we maintain general liability insurance of $5.0 million in the aggregate and clinical trial liability insurance of $10.0 million in the aggregate, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling any product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of any future product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our Financial Position and Need for Additional Capital

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We plan to conduct pre-clinical and non-clinical studies, and to ramp up manufacturing of clinical supplies, of QLS-215 in 2021, and to initiate clinical trials in 2022, and expect that our expenses will increase substantially as a result. In addition, we may in the future initiate new research, preclinical and clinical development efforts for and seek marketing approval for, other product candidates, and would expect our expenses to increase in connection with each of these activities. If we obtain marketing approval for any of our product candidates, we may 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, and these activities would require substantial additional funding. In addition, while we may seek one or more collaborators for future development of our product candidates or programs or for our platform technology, we may not be able to enter into a collaboration for any of our product candidates or programs or for our platform technology on suitable terms or at all. In any event, our existing cash, cash equivalents and short-term investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Furthermore, we have incurred and will continue to incur significant additional costs associated with operating as a public company.

Accordingly, we will be required to obtain substantial additional funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional funding may not be available to us on acceptable terms, on a timely basis or at all, impacting our ability to execute on our strategic plans. Our failure to raise capital on acceptable terms as and when needed may force us to delay, reduce or eliminate our research and development programs or any future efforts to seek approval for and commercialize products, and would have a material adverse effect on our business, results of operations, financial condition and ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and short-term investments are sufficient to support operating expenses through 2023, assuming our stockholders approve the conversion of the Series X Preferred Stock into common stock as discussed further below. Our estimate as to how long we expect our cash, cash equivalents and short-term investments to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. For example, we acquired the QLS-215 program in connection with our merger with Quellis in late January 2021, and our assumptions regarding the funding needed to complete preclinical work, IND-enabling studies, and early stage clinical trials of QLS-215 and manufacturing ramp-up may prove to be inaccurate. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- our ability to integrate QLS-215 into our operations and meet our overall timing expectations for the program;
- the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, QLS-215 any future product candidates, including potential future clinical trials;
- our ability to enter into and the terms and timing of any additional collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, market access, distribution, supply chain and manufacturing capabilities, and scaling up the manufacturing of drug substance and drug product to clinical and commercial scale, securing all raw materials necessary to conduct such scale-up and successfully completing all other activities related thereto;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our product candidates;
- if we obtain marketing approval of any of our products, our ability to successfully compete against other approved products that are approved or used as treatments for the indications for which our products are approved, including with respect to QLS-215 in HAE;
- our headcount growth and associated costs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the impact of the COVID-19 pandemic on our operations, business and prospects; and
- the costs of operating as a public company.

In connection with our acquisition of Quellis, we issued Series X Preferred Stock to Quellis stockholders in the Merger and to the Investors in the February 2021 Financing. We are obligated under the Merger Agreement to seek stockholder approval for the conversion of the Series X Preferred Stock into common stock. In the event that we fail to timely hold the stockholder meeting or fail to obtain stockholder approval, then the holders of the Series X Preferred Stock would be entitled to require us to redeem, in cash, the

shares of common stock underlying their Series X Preferred Stock at a price per share equal to the fair value of the common stock. If we are forced to redeem a significant amount of shares underlying the Series X Preferred Stock, it could, among other things, materially affect our results of operations and cash usage forecasts, require us to slow down or stop the development of QLS-215 and any other future product candidates, require us to raise additional capital and impact our ability to raise additional capital. Also, while we cannot predict the amount with any level of certainty, there is a level of cash settlement at which, if it is exceeded, could require us to make redemption payments in excess of our current liquidity. Based on precedent transactions and the terms of the Series X Preferred Stock, we believe that our stockholders who are entitled to vote on the conversion proposal at our 2021 Annual Meeting of Stockholders, which is scheduled for June 2, 2021, will vote to approve the proposal. However, we cannot be sure that our stockholders will vote to approve the conversion proposal or what the impact will be if they fail to do so. Additionally, as the vote of our stockholders is outside of our control, there is substantial doubt about our ability to continue as a going concern within one year from the filing of this Annual Report on Form 10-K.

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

Our net losses were $37.3 million and $26.3 million for the years ended December 31, 2020 and December 31, 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $260.9 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of preferred stock before we became a public company and our private placement of preferred stock in the February 2021 Financing, registered offerings of our common stock, our at-the-market programs, and a secured debt financing, and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical development programs. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We anticipate that we will continue to incur significant expenses and operating losses and we may incur increased expenses if and to the extent we:

- initiate and continue research and preclinical and clinical development efforts for QLS-215 and any future product candidates;
- seek to identify and develop any future product candidates;
- seek regulatory and marketing approvals for QLS-215 and any future product candidate that successfully completes clinical trials, in the United States and other markets;
- establish sales, marketing, market access, distribution, supply chain and other commercial infrastructure in the future to commercialize products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of QLS-215 and any other future product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio; and
- hire and retain additional personnel or add information systems, equipment or physical infrastructure to support our operations.

To become and remain profitable, we or any potential future collaborators must develop and eventually commercialize at least one product candidate with significant market potential. This will require that we or our collaborators be successful in a range of challenging activities, including completing preclinical studies and clinical trials of one or more product candidates, obtaining marketing approval for one or more these product candidates, manufacturing, marketing and selling those products for which we or our collaborators

may obtain marketing approval and satisfying any post-marketing requirements. We or our collaborators may never succeed in any or all of these activities and, even if we or our collaborators do succeed, we or our collaborators may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause investors to lose all or part of their investments in us.

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

We will need to raise additional capital to develop and commercialize QLS-215 or to acquire, develop and commercialize any future product candidates or to pursue other strategic options. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, our existing stockholders' ownership interests may be substantially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. For example, in connection with the acquisition of Quellis in January 2021 we issued 50,504 shares of Series X Preferred Stock to Quellis stockholders and in the February 2021 Financing, we completed a private placement of 35,573 shares of Series X Preferred Stock. Each share of Series X Preferred Stock is convertible, upon stockholder approval, into 1,000 shares of our common stock. As a result, if such shares of Series X Preferred Stock are converted into common stock, we will issue an aggregate of 86,077,000 shares of our common stock, which will cause substantial dilution of the ownership interests of our existing stockholders. We are obligated to seek stockholder approval of the conversion of the Series X Preferred Stock into common stock and expect to have a stockholders meeting to seek such approval in June 2021. If such conversion is approved, we would expect that a substantial amount of Series X Preferred Stock would automatically convert into shares of our common stock shortly after the approval of the conversion proposal. In addition, our June 2018 and February 2019 registered offerings of common stock and common stock warrants and our January 2020 registered offering of common stock were highly dilutive to existing stockholders' ownership interests. Further, exercise of the common stock warrants sold in our June 2018 and February 2019 offerings, and the warrants that we assumed in the acquisition of Quellis, could result in additional dilution upon exercise.

Debt financing, if available, would result in periodic payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of any future product candidate.

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

Risks Related to Our Dependence on Third Parties

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.

The development and commercialization of product candidates require substantial cash to fund expenses. We may seek one or more collaborators for the development and commercialization of QLS-215 or any future product candidates. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. In addition, any collaboration agreements that we enter into in the future may contain, restrictions on our ability to enter into potential collaborations or to otherwise develop specified compounds.

We face significant competition in seeking appropriate collaborators and strategic partners. Whether we reach a definitive agreement for a collaboration or strategic partnership will depend, among other things, upon our assessment of the other party's resources and expertise, the terms and conditions of the proposed transaction and the proposed party's evaluation of a number of factors. Those factors may include the potential differentiation of ours or a partner's product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator or strategic partner may also be considering alternative transaction types and structures that may be more attractive than the one with us.

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

If we enter into collaborations with third parties for the development and commercialization of a product candidate, our prospects with respect to such product candidate will depend in significant part on the success of those collaborations.

If we enter into collaborations for the development and commercialization of a product candidate, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of such product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of a product candidate or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the market or competitive landscape, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the

research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in negative publicity for our product candidate and the need for additional capital to pursue further development or commercialization of the applicable product candidates.

In addition, all of the risks related to product development, regulatory approval and commercialization described in this "Risk Factors" section would apply to the activities of our collaborators. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination or a sale or other transaction involving our collaboration, it or the party with which it entered into a business combination, sale or other transaction could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

We expect to rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business could be significantly harmed.

We do not plan to independently conduct clinical trials of QLS-215 or any future product candidates. We would expect rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct clinical trials of any such product candidate. Any of these third parties could terminate its engagement with us under certain circumstances or encounter, for example, business challenges, such as a loss of business or the COVID-19 pandemic, or enter into transactions, such as business combinations, that temporarily or permanently impact the amount or type of resources that they are able or willing to devote to our engagement. We might not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could materially impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, our reliance on these third parties for clinical development activities would limit our control over these activities, but we would remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of a product candidate, we would remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or any of our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving a product candidate, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. Many of these risks are heightened by the COVID-19 pandemic. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties that may conduct clinical trials on our behalf would not be our employees, and except for remedies available to us under our agreements with such contractors, we would not be able to

control whether or not they devote sufficient time, skill and resources to our development programs, a risk that would potentially be exacerbated during the COVID-19 pandemic as any such third parties try to address the impact of the pandemic on their own businesses and financial condition. Any such contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for the applicable product candidates. If that occurs, we would not be able to, or may be delayed in our efforts to, successfully commercialize such product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be impaired.

We also expect to rely on other third parties to store and distribute drug supplies for any future clinical trials we may pursue. Any performance failure on the part of any such distributors could delay clinical development or marketing approval of any future product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

The manufacturing of pharmaceutical products and, in particular, biologics, is complex and we do not have our own clinical manufacturing capabilities. We will rely on third parties to produce clinical and commercial supplies of any future product candidates.

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We plan to rely on third-party contract manufacturers to manufacture all of our preclinical product candidate supplies and clinical trial product supplies. We do not own, nor do we plan to own, any manufacturing facilities. There can be no assurance that our preclinical and clinical development product supplies from third parties will not be limited or interrupted, or be of satisfactory quality or continue to be available at acceptable prices. Additionally, the process of manufacturing pharmaceutical products and, in particular, biologics is complex, highly regulated, and subject to multiple risks. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, other supply disruptions and higher costs. If microbial, viral or other contaminations are discovered at the facilities of our third-party contract manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials, result in higher costs of drug product and adversely affect our business.

If the contract manufacturers we engage are unable to supply us with sufficient clinical grade quantities of our product candidates, and we are unable to timely establish an alternate supply from one or more third-party contract manufacturers, we will experience delays in our development efforts as we seek to locate and qualify new manufacturers. In particular, any replacement of our third-party contract manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements or capacity could be limited at each of the qualified replacements. We expect to obtain drug product and drug substance from single third party sources, which exacerbates these and other related risks for us. Additionally, contract manufacturers may rely on single source suppliers for certain of the raw materials for our preclinical and clinical product supplies. If current or future suppliers are delayed or unable to supply sufficient raw materials to manufacture product for our preclinical studies and clinical trials, we may experience delays in our development efforts as materials are obtained or we locate and qualify new raw material manufacturers.

The manufacturing process for a clinical candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with their standards, such as cGMPs. In the event that any of our manufacturers fail to comply with such requirements or to perform their 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. The transfer of the manufacturing of biologic products to a new contract manufacturer and any additional process development that may be necessary can be lengthy and involve significant additional costs. 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 would negatively affect our ability to develop product candidates in a timely manner or within budget.

Further, our reliance on third-party manufacturers exposes us to risks beyond our control, including the:

- inability to meet our drug specifications and quality requirements consistently;
- inability to initiate or continue preclinical studies or clinical trials of product candidates under development;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and drug quality issues, including related to scale-up of manufacturing;
- failure to comply with cGMP and similar foreign standards;
- reliance on a limited number of sources, and in some cases, potentially single sources for drug components and raw materials, such that if we are unable to secure a sufficient supply of these drug components and raw materials, we will be unable to manufacture and sell our future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components and raw materials that are purchased from a sole or single source supplier;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- disruption of operations by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or the issuance of an FDA Form 483 notice or warning letter;
- carrier disruptions or increased costs that are beyond our control;
- failure to deliver our drugs under specified storage conditions and in a timely manner; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production, any of which could result in a failure to begin our clinical trials or having to stop ongoing clinical trials. In addition, our third-party manufacturers and suppliers are subject to FDA inspection from time to time. Failure by our third-party manufacturers and suppliers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidate may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of the regulatory action, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

In addition, our contract manufacturers are or may be engaged with other companies to supply and manufacture materials or products for such companies, which also exposes our suppliers and manufacturers

to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility, which could impact the contract supplier's or manufacturer's ability to manufacture drug product for us.

Risks Related to Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to QLS-215 and any future product candidates. If we do not adequately protect our intellectual property, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have filed a provisional United States patent application directed to QLS-215 and intend to file patent applications in the United States and abroad related to QLS-215 and future novel product candidates and related technologies that are important to our business. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Failure to protect or to obtain, maintain or extend adequate patent and other intellectual property rights could materially adversely affect our ability to develop and market our products and product candidates. The enforcement, defense and maintenance of such patents and other intellectual property rights may be challenging and costly.

We cannot be certain that any patent application directed to QLS-215 or any future product candidate will be issued in a form that provides us with adequate protection to prevent competitors from developing competing products. As a biopharmaceutical company, our patent position is uncertain because it involves complex legal and factual considerations. The standards applied by USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biopharmaceutical patents. Consequently, patents may not issue from any applications that are currently pending or that we file in the future. As such, we do not know the degree of future protection that we will have for QLS-215 and related technologies. The scope of patent protection that the USPTO and foreign patent offices will grant with respect to QLS-215 is uncertain. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. For example, it is possible that the USPTO and foreign patent offices will not allow broad antibody claims that specifically cover our QLS-215 product candidate and antibodies closely related to it. As a result, upon receipt of FDA approval, or regulatory approval in foreign jurisdictions, competitors may be free to market antibodies almost identical to ours, including biosimilar antibodies, thereby decreasing our market share. However, a competitor cannot submit to the FDA an application for a biosimilar product based on QLS-215 or any future biologic products until four years following the date of approval of our "reference product," and the FDA may not approve such a biosimilar product until 12 years from the date on which the reference product was approved. See the section of this Annual Report on Form 10-K entitled "Business — Government Regulation and Product Approval — Biosimilars" for more details regarding biosimilar regulatory exclusivities.

Our pending provisional patent application and any future patent applications we file cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, patents are granted to the party who was the first to file a patent application. However, prior to March 16, 2013, in the United States, patents were granted to the party who was the first to invent the claimed subject matter. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third party preissuance submission of prior art to the USPTO, or become involved in post-grant review procedures, oppositions, derivations, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing antibodies or compounds similar or identical to our product candidates, or limit the duration of the patent protection of our product candidates. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Patent applications may not result in patents being issued which protect any current and future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

Even if patent applications that we file issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with any of our future products. Alternatively, our competitors may seek to market biosimilar versions of any approved products by submitting an application for a biosimilar product under the BPCIA. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

If we do not obtain protection under the Hatch-Waxman Act and similar non-United States legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Patents have a limited duration. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, their manufacture, or use are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our United States patents, if issued, may be eligible for limited patent term extension under the Hatch-Waxman Act, or under similar legislation in other countries. The Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. The patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or

the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner than we expect. As a result, our revenue from applicable products could be reduced, possibly materially.

Our development and commercialization rights to QLS-215 and future product candidates and technology may be subject, in part, to the terms and conditions of licenses granted to us by others.

We may become reliant upon licenses to certain patent rights and proprietary technology from third parties that are relevant to our QLS-215 product candidate and possible future product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we choose to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses.

Such license agreements would likely impose various development obligations, payment of royalties and fees based on achieving certain milestones, as well as other obligations. In addition, our licensors, in the future, may allege that we have materially breached our obligations under a certain license agreement and may therefore terminate that license agreement. If we fail to comply with our obligations under these agreements, the licensor may have the right to terminate the license. The termination of any such license agreements or failure to adequately protect such license agreements could prevent us from commercializing product candidates covered by the licensed intellectual property. Furthermore, our competitors may obtain the freedom to seek regulatory approval of, and to market products competitive with ours.

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 any collaboration relationships we might enter into in the future;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know how resulting from the joint creation or use of intellectual property by our licensors and us; and
- the priority of invention of patented technology.

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

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our

ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

An intellectual property litigation could lead to unfavorable publicity that could harm our reputation and cause the market price of our common stock to decline.

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. In such event, the market price of our common stock may decline.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing current and future product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell QLS-215, as well as any future product candidates, without infringing the intellectual property and other proprietary rights of third parties. If any third-party patents or patent applications are found to cover QLS-215 or any future product candidates or their methods of use, we may not be free to manufacture or market such product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

In spite of our efforts to avoid obstacles and disruptions arising from third-party intellectual property, it is impossible to establish with certainty that our programs directed to QLS-215 and any future product candidates will be free of claims by third-party intellectual property holders. Even with modern databases and on-line search engines, literature searches are imperfect and may fail to identify relevant patents and published applications. Even when a third-party patent is identified, we may conclude upon a thorough analysis, that we do not infringe the patent or that the patent is invalid. If the third-party patent owner disagrees with our conclusion and we continue with the business activity in question, patent litigation may be initiated against us. Alternatively, we might decide to initiate litigation in an attempt to have a court declare the third-party patent invalid or non-infringed by our activity. In either scenario, patent litigation typically is costly and time-consuming, and the outcome is uncertain. The outcome of patent litigation is subject to uncertainties that cannot be quantified in advance, for example, the credibility of expert witnesses who may disagree on technical interpretation of scientific data. Ultimately, in the case of an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our technology platform as a result of patent infringement claims asserted against us. This could have a material adverse effect on our business.

There is a substantial amount of intellectual property litigation in the biopharmaceutical industry, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to QLS-215 or any future product candidates, including interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The biopharmaceutical industry has produced a significant

number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that any current or future product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

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

Our involvement in litigation, and in, e.g., any interference, derivation, reexamination, inter partes review, opposition or post-grant proceedings or other intellectual property proceedings in the United States, or other jurisdictions, may divert management time from focusing on business operations, could cause us to spend significant amounts of money and may have no guarantee of success. Any current and potential intellectual property litigation also could force us to do one or more of the following:

- stop selling, manufacturing or using our products in the United States or other jurisdictions that use the subject intellectual property;
- obtain from a third party asserting its intellectual property rights, a license to sell or use the relevant technology, which license may not be available on reasonable terms, or at all, or may be non-exclusive thereby giving our competitors access to the same technologies licensed to us;
- redesign those products or processes that use any allegedly infringing or misappropriated technology, which may result in significant cost or delay to us, or which redesign could be technically infeasible; or
- pay damages, including the possibility of treble damages in a patent case if a court finds us to have willfully infringed certain intellectual property rights.

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

Along with patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, contract research organizations, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants.

Trade secrets and confidential know-how are difficult to maintain as confidential. Although we use reasonable efforts to protect our trade secrets, any party with whom we have executed a confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Accordingly, we may not be able to obtain adequate remedies for such breaches, despite any legal action that we might take against persons making such unauthorized disclosures. In addition, courts outside the United States sometimes are less willing than United States courts to protect trade secrets.

If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Those with whom we collaborate on research and development related to current and future product candidates may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law in September 2011, could increase those uncertainties and costs. The Leahy-Smith Act included a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, for example, via post grant review and inter partes review proceedings at the USPTO. In addition, the Leahy-Smith Act transformed the United States patent system into a "first to file" system. The first-to-file provisions, however, only became effective in March 2013. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The United States 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 United States Congress, the United States courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in 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.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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

- others may be able to make antibodies that are the same as or similar to QLS-215 or future product candidates but that are not covered by the claims of patents that we own or have rights to;

- we or our licensors or any current or future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by our pending patent application;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent rights will not lead to issued patents, or that patents, if granted, may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our products or technologies could use the intellectual property of others without obtaining a proper license;
- we may not develop additional technologies that are patentable; and
- third parties may allege that our development and commercialization of QLS-215 or future products may infringe their intellectual property rights, the outcome of which may have an adverse effect on our business.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO 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. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering any future product candidates, our competitive position would be adversely affected.

We may obtain only limited geographical protection with respect to certain patent rights, which may diminish the value of our intellectual property rights in those jurisdictions and prevent us from enforcing our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive. Accordingly, we may not file for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national/regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The requirements for patentability may differ in certain countries, particularly in developing countries. 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 may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed

patents or where any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing with us.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business, results of operations and financial condition may be adversely affected. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. 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, if our ability to enforce our patents to stop infringing activities in those jurisdictions is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at other biopharmaceutical companies, including our competitors or potential competitors. Some of these employees, including members of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, and Quellis did the same, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of QLS-215 or any future product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of biopharmaceutical products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, which regulations differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we, or they, receive approval of a BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Product candidates in the development phase are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have no experience as a company in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

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

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. This may be exacerbated during the COVID-19 pandemic as FDA focuses its resources on vaccines and other treatments for COVID-19. In addition. over the last several years, the United States government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

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

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we may be granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions and any of our product candidates that may be approved for marketing in a foreign jurisdiction will be subject to risks associated with foreign operations.

In order to market and sell our products in the European Union and other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements.

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

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

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom and European Union entered into a Trade and Cooperation Agreement in connection with Brexit that sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for any future product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We, or any future collaborators, may seek orphan drug designations and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the

applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because FDA has taken the position that, under certain circumstances, another drug with the same active moiety can be approved for the same condition. Specifically, the FDA's regulations provide that it can approve another drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

In 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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

Any product candidate for which we obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. Accordingly, if we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

We must also comply with requirements concerning advertising and promotion for any product candidate for which we obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

We may seek certain designations for our product candidates, including Breakthrough Therapy, RMAT Therapy, Fast Track and Priority Review designations, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy and Regenerative Medicine Advanced Therapy, or RMAT, product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough and RMAT therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We and our contract manufacturers are subject to significant regulation. The manufacturing facilities on which we rely may not continue to meet regulatory requirements, which could materially harm our business.

All entities involved in the preparation of product candidates for clinical trials or commercial sale, including any contract manufacturers, are subject to extensive regulation. 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 must adhere to the FDA's current Good Laboratory Practice and cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our contract manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of any product candidate. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our contract manufacturers. If any such inspection or audit identifies 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, which may lead to temporary or permanent supply shortages. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product, or revocation of a pre-existing approval. Any such consequence would severely harm our business, financial condition and results of operations.

Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for any of our product candidates that do receive marketing approval.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the United States Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked those Orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Current and future legislative efforts may limit prices for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent United States congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction. It remains to be seen whether these

orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Potentially applicable United States federal and state healthcare laws and regulations include the following:

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

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or qui tam actions 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.

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare

benefit program. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

False Statements Statute. 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.

Transparency Requirements. 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 the United States Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.

Analogous State and Foreign Laws. 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 manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our 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.

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 subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

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 operate or plan to operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal

health data, is subject to the European Union General Data Protection Regulation, or the GDPR, which took effect across all member states of the EEA in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including strict rules on the transfer of personal data to countries outside the European Union, including the United States.

As a result, there is increased scrutiny on the extent to which clinical trial sites located in the EEA should apply the GPDR to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar initiatives are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with such requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, 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 and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We are subject to United States and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the United States Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the United States domestic bribery statute contained in 18 U.S.C. § 201, the United States Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary

permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. If any subpoenas, investigations or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Further, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, CROs, consultants, commercial partners, vendors and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Even with appropriate policies and procedures, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives that could harm our business.

The commercial success of any future product that we may develop will depend substantially, both domestically and abroad, on the extent to which the costs of such product will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize such product. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Many countries outside the United States, including many countries in the European Union, require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and can be lengthy, involve extensive negotiations and potentially result in price caps, significant discounts or other budgetary control measures, which could correspondingly impact pricing and reimbursement in other markets through so-called informal or formal reference pricing schemes. These reviews and negotiations could ultimately result in a pricing and reimbursement structure for a drug that a company deems inadequate and therefore elects not launch in such markets. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if any future product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any product will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell any products we develop profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for any future products decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. For example, to obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any product candidate for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Risks Related to Taxation

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us and our stockholders. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, a limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), a limitation of the deduction for net operating losses to 80% of current year taxable income and an elimination of net operating loss carrybacks (though any net operating losses generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely), and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or the FFCR Act, was enacted on March 18, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was enacted on March 27, 2020, and COVID relief provisions were included in

the Consolidated Appropriations Act, 2021 or CAA, which was enacted on December 27, 2020. All contain numerous tax provisions. In particular, the CARES Act, among other things, suspends the 80% limitation on the deduction for net operating losses in taxable years beginning before January 1, 2021, permits a 5-year carryback of net operating losses arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted taxable income for taxable years beginning in 2019 and 2020.

It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, and as a result of the changes in the U.S. presidential administration and control of the U.S. Senate, additional tax legislation may also be enacted. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in the combined company's or the combined company's stockholders' tax liability or require changes in the manner in which the combined company operates in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our ability to use net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

In general, under Sections 382 and 383 of the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. As a result of the shares issued in January and February 2021 related to the acquisition of Quellis and the concurrent private placement of Series X Preferred Stock, we have likely experienced an ownership change, as defined by Section 382. If we have experienced an ownership change, as defined by Section 382, at any time since inception, utilization of the federal and state net operating loss carryforwards or research and development tax credit carryforwards would be subject to annual limitation under Sections 382 and 383. Under Section 382, the annual limitation is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. We are planning to complete a study to confirm an ownership change occurred in 2021 and assess whether there have been multiple ownership changes since inception, as well as the resulting amount of the limitation on our net operating loss carryforwards and research and development tax credit carryforwards. In addition, our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits.

Risks Related to Employee Matters, Managing Growth and Information Technology

Our future success depends on our ability to retain our senior management and key employees.

We are highly dependent on our executive officers and key employees. If we are unable to retain our executive officers or other key employees, replacing them may be difficult and may take an extended period of time because of the nature of our current business strategy and the limited number of individuals in our industry with the relevant breadth of skills and experience. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate replacements for our executive officers or key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

We rely on consultants and advisors, including financial, legal, scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us.

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

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information, employee data and personally identifiable information of clinical trial participants in accordance with informed consents covering such information. We also rely to a large extent on information technology systems to operate our business. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure, and that of our vendors and third-party providers, may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our vendors and third-party providers could be susceptible to third party attacks on our and their information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. While we have invested in information technology security measures and the protection of confidential information, there can be no assurance that our efforts will prevent service interruptions or security breaches. For example, we have detected common types of attempts to attack our information technology systems and data using means that have included phishing. Any service interruptions or security breaches of our information technology systems may substantially impair our ability to operate our business and could compromise our networks, or those of our vendors and third-party providers, and the information stored could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business.

Risks Related to Our Common Stock

Pursuant to the terms of the Merger Agreement, we are required to recommend that our stockholders approve the conversion of all outstanding shares of our Series X Preferred Stock into shares of our common stock. We cannot guarantee that our stockholders will approve this matter, and if they fail to do so our operations may be materially harmed.

Under the terms of the Merger Agreement, we agreed to use commercially reasonable efforts to call and hold a meeting of our stockholders to obtain the requisite approval for the conversion of all outstanding shares of Series X Preferred Stock issued in the Merger and February 2021 Financing into shares of our common stock, as required by the Nasdaq listing rules, within 180 days after the date of the Merger Agreement and, if such approval is not obtained at that meeting, to seek to obtain such approval at an annual or special stockholders meeting to be held at least every six months thereafter until such approval is obtained, which would be time consuming and costly. Additionally, if our stockholders do not timely approve the conversion of our Series X Preferred Stock, then the holders of the Series X Preferred Stock would be entitled to require us to redeem, in cash, the shares of common stock underlying their Series X Preferred Stock at a price per share equal to the fair value of the common stock. If we are forced to redeem a significant amount of shares underlying the Series X Preferred Stock, it could, among other things, materially affect our results of operations and cash usage forecasts, require us to slow down or stop the development of QLS-215 and any other future product candidates, require us to raise additional capital and impact our ability to raise additional capital. Also, while we cannot predict the amount with any level of certainty, there is a level of cash settlement at which, if it is exceeded, could require us to make redemption payments in excess of our current liquidity. Based on precedent transactions and the terms of the Series X Preferred Stock, we believe that our stockholders who are entitled to vote on the conversion proposal at our 2021 Annual Meeting of Stockholders, which is scheduled for June 2, 2021, will vote to approve the proposal. However, we cannot be sure that our stockholders will vote to approve the conversion proposal or what the impact will be if they fail to do so. Additionally, as the vote of our stockholders is outside of our control, there is substantial doubt about our ability to continue as a going concern within one year from the filing of this Annual Report on Form 10-K.

The price of our common stock has been and is likely to continue to be highly volatile, which could result in substantial losses for our stockholders.

Our stock price has been and is likely to continue to be highly volatile. For example, when we announced our acquisition of Quellis, our stock price increased by approximately 70% in one day. In the twelve months ending February 26, 2021, the last business day in February, our stock price has traded at a high of $8.59 and a low of $1.25.

The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our investors may lose some or all of their investments. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of QLS-215 or any future product candidate;
- commencement or termination of collaborations for any development programs we may pursue;
- failure or discontinuation of any of any development programs we may pursue;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to a product candidate or clinical development program;
- the results of any additional efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or recommendations by securities analysts that cover our stock;
- announcement or expectation of additional financing efforts;
- announcement of collaborations, licenses, acquisitions or other comparable forms of transactions;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including political instability, or instability from an outbreak of pandemic or contagious disease, such as the ongoing COVID-19 pandemic; and
- the other factors described in this "Risk Factors" section.

Additionally, securities class action litigation has often been brought against a company following a decline in the market price of its securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

As a public company we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that our management and other personnel will continue to devote

a substantial amount of time towards maintaining compliance with these requirements. These requirements increase our legal and financial compliance costs and make some activities more time-consuming and costly. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of SOX, we are required to furnish reports by our management on our internal control over financial reporting with our Annual Reports on Form 10-K with the SEC. If we cease to be a smaller reporting company with less than $100 million in annual revenue, we will also be required to include attestation reports on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404 of SOX. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of February 28, 2021, we had outstanding 23,417,006 shares of common stock, 3,332,669 of which shares were issued at the closing of the Merger. As of February 28, 2021, we also had outstanding 86,077 shares of our Series X Preferred Stock issued at the closing of the Merger and in the February 2021 Financing, which are convertible into 86,077,000 shares of our common stock. The holders of shares of common stock issued at the closing of the Merger and the holders of shares of Series X Preferred Stock are entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act. Registration of these shares under the Securities Act will result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any significant sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

As of February 28, 2021, we also had outstanding warrants to purchase 4,200,000 shares of common stock at an exercise price of $12.00 per share, and 1,991,300 shares of common stock at an exercise price of $6.25 per share. These warrants are fully exercisable and remain exercisable for five years from their respective dates of issuance, and we have registered the issuance of shares upon exercise of these warrants under registration statements. As a result, the shares issuable upon exercise of these warrants can be freely sold in the public marked upon issuance, subject to volume limitations applicable to affiliates. Sales of these shares could cause the market price of our common stock to decline significantly. Furthermore, if our stock price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our common stock and reduce or eliminate any appreciation in our stock price that might otherwise occur.

Additionally, we have an ongoing sales agreement with Cowen and Company LLC, pursuant to which we could issue and sell shares of common stock under at-the-market offering programs.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future, accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. Any future

debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be investors' sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will likely depend, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

Risks Relating to our Certificate of Incorporation and Bylaws

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

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

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

In addition, we issued 86,077 shares of our Series X Preferred Stock in connection with the acquisition of Quellis and the February 2021 Financing. Except as otherwise required by law, the Series X Preferred Stock does not have voting rights. However, as long as any shares of Series X Preferred Stock are outstanding, we may not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series X Preferred Stock, (i) alter or change adversely the powers, preferences or rights given to the Series X Preferred Stock or alter or amend the Certificate of Designation that authorized the Series X Preferred Stock, amend or repeal any provision of, or add any provision to, our Certificate of Incorporation or bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and

relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series X Preferred Stock, (ii) issue further shares of Series X Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series X Preferred Stock, or (iii) enter into any agreement with respect to any of the foregoing. Additionally, the approval of the holders of a majority of the Series X Preferred Stock is required for certain change of control transactions, provided that this approval right will terminate upon stockholder approval of the Conversion Proposal.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Our certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or any action asserting a claim against us governed by the internal affairs doctrine. These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers, or employees, which may discourage such lawsuits against us and our directors, officers, and employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition, and operating results. This exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act, which provides for exclusive jurisdiction of the federal courts. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder; provided, that with respect to claims under the Securities Act, our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our offices are located in Boston, Massachusetts and consist of approximately 11,000 square feet of subleased office space under a lease that expires in July 2022. We believe that our existing facilities are sufficient for our needs for the foreseeable future.

Item 3. Legal Proceedings

From time to time we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this Annual Report on Form 10-K, we do not believe we are party to any

claim or litigation, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

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, $0.001 par value per share, has been publicly traded on the Nasdaq Global Market under the symbol "CATB" since June 25, 2015. Prior to that time, there was no public market for our common stock.

Holders

As of March 4, 2021, there were approximately 29 holders of record of our common stock. This number of holders of record does not include beneficial owners of our common stock whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

We did not sell or issue any equity securities that were not registered under the Securities Act during the period covered by this Annual Report on Form 10-K.

As described elsewhere in this Annual Report on Form 10-K, on January 28, 2021, we acquired Quellis pursuant to the Merger Agreement. Under the terms of the Merger Agreement, at the closing of the Merger, we issued to the Quellis stockholders 3,332,669 shares of our common stock and 50,504 shares of newly designated Series X Preferred Stock. In addition, we assumed outstanding Quellis stock options, which became options for our common stock, and assumed a warrant exercisable for Quellis common stock, which became a warrant to purchase 2,805 shares of Series X Preferred Stock at an exercise price of $341.70 per share, and a warrant to purchase 185,136 shares of common stock at an exercise price of $0.35 per share.

On February 1, 2021, we closed the February 2021 Financing pursuant to which we sold an aggregate of 35,573 shares of Series X Preferred Stock for an aggregate purchase price of $110.0 million. Subject to stockholder approval, each share of Series X Preferred Stock issued in the Merger and pursuant to the Purchase Agreement is convertible into 1,000 shares of common stock. Pursuant to the Merger Agreement, we have agreed to hold a stockholders' meeting to submit the approval of the conversion of the Series X Preferred Stock into shares of our common stock in accordance with Nasdaq Listing Rule 5635(a), or the Conversion Proposal. Assuming stockholder approval of the Conversion Proposal, on the fourth business day after such approval, each share of Series X Preferred Stock then outstanding would automatically convert into 1,000 shares of common stock, subject to certain beneficial ownership limitations, including that a holder of Series X Preferred Stock is prohibited from converting shares of Series X Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (to be initially set at 9.99% and thereafter adjusted by the holder between to a number between 4.99% and 19.99%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion.

Also, on January 28, 2021, we entered into a Registration Rights Agreement, or the Registration Rights Agreement, with the holders of common stock issued in the Merger and the holders of Series X Preferred Stock. Pursuant to the Registration Rights Agreement, we will prepare and file a resale registration statement with the SEC within 90 calendar days following the February 1, 2021 closing of the Financing, or the Filing Deadline. We will use our reasonable best efforts to cause this registration statement to be

declared effective by the SEC within 30 calendar days of the Filing Deadline (or within 60 calendar days if the SEC reviews the registration statement).

Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Selected Financial Data

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics. Our mission is to bring hope with life-changing therapies to patients and families that are affected by rare diseases. Our lead product candidate is QLS-215, a potential best-in-class monoclonal antibody inhibitor of plasma kallikrein in preclinical development for the treatment of hereditary angioedema, or HAE, a rare, debilitating and potentially life-threatening disease.

In January 2021, as further described below, we acquired Quellis Biosciences, Inc., or Quellis, including the QLS-215 program, and announced a private placement that, upon closing in February 2021, resulted in gross proceeds to us of approximately $110.0 million before deducting placement agent and other offering expenses. In November 2020, after we stopped the development of our edasalonexent program as a potential treatment for Duchenne Muscular Dystrophy, or DMD, we decided to explore and evaluate strategic options and engaged Ladenburg Thalmann & Co., Inc. as our strategic financial advisor. The acquisition of Quellis was the result of our evaluation of strategic options and we believe that the acquisition represents an opportunity to create substantial value for our stockholders.

HAE is a rare, debilitating and potentially life-threatening disease. The treatment options for patients with HAE have improved, however there is remaining unmet medical need and the global market for HAE therapy is strong and growing. The vision for our lead program, QLS-215, is to develop a best-in-class monoclonal antibody inhibitor of plasma kallikrein for HAE prophylaxis that is able to treat HAE by achieving sustained blood levels of QLS-215 with infrequent dosing. Plasma kallikrein is a critical component of HAE that causes pathologic vascular permeability, vasodilation and ultimately excessive tissue swelling. QLS-215 is a humanized monoclonal antibody targeting plasma kallikrein that has shown in preclinical studies that it may potentially enable patients to dose less frequently and potentially be more effective than existing HAE treatments. QLS-215 is currently in preclinical development and we expect to submit an Investigational New Drug application, or IND, for QLS-215 in the first half of 2022 and plan to initiate a Phase 1a clinical trial with initial results anticipated by the end of 2022. Subsequently, assuming positive data from the Phase 1a clinical trial, we plan to initiate a Phase 1b/2 trial in patients with HAE in 2023 with initial results anticipated by the end of 2023. We believe that these clinical trials have the opportunity to establish proof of concept for the differentiated profile of QLS-215.

Previously, our lead program was edasalonexent, which was in Phase 3 clinical development for the treatment of DMD. In October 2020, we announced that the Phase 3 PolarisDMD trial of edasalonexent did not meet its primary endpoint, which was a change from baseline in the North Star Ambulatory Assessment over one year of treatment with edasalonexent compared to placebo. In addition, we announced that the secondary endpoint timed function tests (time to stand, 10-meter walk/run and 4-stair climb) did not show statistically significant improvements. Based on these results, we stopped activities related to the development of edasalonexent, including the GalaxyDMD open-label extension trial. The Phase 3 Polaris DMD trial was a one-year placebo-controlled trial designed to evaluate the safety and efficacy of edasalonexent in boys ages 4-7 (up to 8th birthday) with DMD. The trial enrolled 131 boys across eight countries, with any mutation type, who were not on steroids. Edasalonexent was well-tolerated, consistent with the safety profile seen to date. The majority of adverse events were mild in nature and the most common treatment-related adverse events were diarrhea, vomiting, abdominal pain and rash. There were no treatment-related serious adverse events and no dose reductions. Data from the Phase 3 PolarisDMD trial will be further analyzed and we expect to publish these data.

January 2021 Quellis Acquisition and February 2021 Financing

In January 2021, we acquired Quellis pursuant to an Agreement and Plan of Merger, or the Merger Agreement, by and among us, Cabo Merger Sub I, Inc., a Delaware corporation and our wholly owned subsidiary, or the First Merger Sub, Cabo Merger Sub II, LLC, a Delaware limited liability company and our wholly owned subsidiary, or the Second Merger Sub, and Quellis. Pursuant to the Merger Agreement, the First Merger Sub merged with and into Quellis, pursuant to which Quellis was the surviving entity and became a wholly owned subsidiary of Catabasis, or the First Merger. Immediately following the First Merger, Quellis merged with and into the Second Merger Sub, pursuant to which the Second Merger Sub was the surviving entity, or the Second Merger and, together with the First Merger, the Merger. Under the terms of the Merger Agreement, at the closing of the Merger, we issued to the Quellis stockholders 3,332,669 shares of our common stock, and 50,504 shares of newly designated Series X Preferred Stock (as described below). In addition, we assumed outstanding Quellis stock options, which became options for our common stock, and assumed a warrant exercisable for Quellis common stock, which became a warrant to purchase 2,805 shares of Series X Preferred Stock at an exercise price of $341.70 per share, and a warrant to purchase 185,136 shares of our common stock at an exercise price of $0.35 per share.

In January 2021, we also entered into a Stock Purchase Agreement, or the Purchase Agreement, with certain institutional and accredited investors, or the Investors, pursuant to which, we sold an aggregate of 35,573 shares of Series X Preferred Stock for an aggregate purchase price of $110.0 million, or the February 2021 Financing. Subject to stockholder approval, each share of Series X Preferred Stock issued in the Merger and pursuant to the Purchase Agreement is convertible into 1,000 shares of common stock. Pursuant to the Merger Agreement, we have agreed to hold a stockholders' meeting to submit the following matters to our stockholders for their consideration: (i) the approval of the conversion of the Series X Preferred Stock into shares of common stock in accordance with Nasdaq Listing Rule 5635(a), or the Conversion Proposal and (ii) if necessary or appropriate, the approval of an amendment to our certificate of incorporation to authorize sufficient shares of common stock after the conversion of the Series X Preferred Stock issued pursuant to the Merger Agreement and the Purchase Agreement and/or to effectuate a reverse stock split, or the Charter Amendment Proposal. Assuming stockholder approval of the Conversion Proposal, on the fourth business day after such approval, each share of Series X Preferred Stock then outstanding would automatically convert into 1,000 shares of common stock, subject to certain beneficial ownership limitations, including that a holder of Series X Preferred Stock is prohibited from converting shares of Series X Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (to be initially set at 9.99% and thereafter adjustable by the holder to a number between 4.99% and 19.99%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion. Shares of Series X Preferred Stock not converted automatically are thereafter subject to conversion at the option of the holder.

Financial Overview

Revenue

As of December 31, 2020, we have not generated any revenue from product sales.

Research and Development Expenses

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

- employee-related expenses including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations that conduct clinical trials and research and development and preclinical activities on our behalf;
- the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing study materials; and

- facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

We typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or external consultant costs to specific product candidates or development programs. We record our research and development expenses net of any research and development tax incentives we are entitled to receive from government authorities.

The following table summarizes our research and development expenses by program (in thousands). All of the programs with respect to which we incurred research and development expenses during the years ended December 31, 2020 and 2019 have been discontinued.

	Year Ended December 31,	
	2020	2019
Edasalonexent	$17,344	$11,973
CAT-5571	12	15
Costs not directly allocated to programs:		
Employee expenses including cash compensation, benefits and stock-based compensation	6,101	5,062
Facilities	515	303
Consultants and professional expenses, including stock-based compensation	1,134	602
Other	484	362
Total costs not directly allocated to programs	8,234	6,329
Total research and development expenses	$25,590	$18,317

Since inception of the edasalonexent and the CAT-5571 programs, total direct expenses to support the programs have been $66.8 million and $4.2 million, respectively.

Based on the results of the Phase 3 PolarisDMD trial of edasalonexent for the treatment of DMD, we stopped all activities related to the development of edasalonexent, including the ongoing GalaxyDMD open-label extension trial.

We expect to incur significant research and development expenses in the year ending December 31, 2021 and in future periods in connection with the preclinical and clinical activities related to the development of QLS-215. Because of this, we expect that our research and development expenses will be fairly consistent over the next several quarters as compared to the prior year periods. Development of QLS-215 and any future product candidates is highly uncertain and we cannot reasonably estimate at this time the nature, timing and costs of the efforts that would be necessary to complete the development of any such product candidates. We are also unable to predict when, if ever, material net cash inflows would commence from any such product candidates. This is due to the fact that we would need to raise substantial additional capital to fund the clinical development of any such product candidates and the numerous risks and uncertainties associated with developing product candidates, including the uncertainties of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- launching commercial sales, if and when we are able to obtain marketing approval, whether alone or in collaboration with others; and
- a continued acceptable safety profile following approval.

A change in the outcome of any of these variables with respect to the development of QLS-215 or any future product candidate would significantly change the costs and timing associated with the development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, commercial, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that in the near term our general and administrative expenses will remain relatively consistent with their current levels, although as we continue to develop QLS-215 and potentially expand our pipeline to include other product candidates, our general and administrative expenses may increase.

Reduction in Workforce

In December 2020, following the decision to stop development of edasalonexent, we announced that we were reducing our workforce during the quarter ended December 31, 2020. Charges for employee severance and employee benefits of $0.4 million were recorded in the year ended December 31, 2020, all of which will be paid in 2021. Substantially all of these costs were recorded in the research and development section of the accompanying consolidated statement of operations.

Other Income (Expense)

Other income (expense), net consists of interest income earned on our cash, cash equivalents and short-term investments and net amortization expense on short-term investments, and gains and losses related to foreign currency fluctuations.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policy is the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing contracts, identifying services that have been performed on our

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

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting expense amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

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, together with the dollar change in those items (in thousands):

	Year Ended December 31,		
	2020	2019	Period-to-Period Change
Operating expenses:			
Research and development	$ 25,590	$ 18,317	$ 7,273
General and administrative	11,845	8,771	3,074
Total operating expenses	37,435	27,088	10,347
Loss from operations	(37,435)	(27,088)	(10,347)
Other income, net	135	795	(660)
Net loss	$(37,300)	$(26,293)	$(11,007)

Research and Development Expenses

Research and development expenses increased by $7.3 million to $25.4 million for the year ended December 31, 2020 from $18.3 million for the year ended December 31, 2019, an increase of 40%. The increase in research and development expenses was attributable to activities associated with conducting the Phase 3 PolarisDMD clinical trial, the GalaxyDMD open label extension, and regulatory and manufacturing preparations for advancing the edasalonexent program prior to receiving the Phase 3 results. The $7.3 million increase consisted of a $5.4 million increase in direct program costs to support our edasalonexent program, a $1.1 million increase in employee expenses, a $0.5 million increase in consulting and professional services, a $0.2 million increase in the research and development portion of facilities expense and a $0.1 million increase in the research and development portion of other miscellaneous office expenses.

General and Administrative Expenses

General and administrative expenses increased by $3.1 million to $11.9 million for year ended December 31, 2020 from $8.8 million for the year ended December 31, 2019, an increase of 35%. The

increase in general and administrative expenses was attributable to a $1.8 million increase in consulting and professional services primarily related to an increase in preparations for potential commercialization of edasalonexent, a $0.6 million increase in employee expenses, a $0.3 million increase in insurance expense, a $0.2 million increase in the general and administrative portion of facilities expense, and a $0.2 million increase in other miscellaneous office expenses.

Other Income (Expense), Net

Other income (expense), net decreased by $0.7 million for the year ended December 31, 2020 compared to the year ended December 31, 2019, which was attributable to a decrease in interest and investment income due to lower interest rates.

Liquidity and Capital Resources

From our inception through December 31, 2020, we raised an aggregate of $316.0 million, through various private placements of preferred stock, our initial public offering, as well as various other registered equity offerings, including underwritten public offerings, at-the-market programs, and stock option and warrant exercises. As of December 31, 2020, we had $44.9 million in cash, cash equivalents and short-term investments. Subsequent to December 31, 2020, we raised an additional $110.0 million in gross proceeds from the February 2021 Financing.

We have not generated any revenue from product sales to date. We have incurred significant annual net operating losses in every year since our inception and expect to incur net operating losses in 2021 and for the foreseeable future. As of December 31, 2020, we had an accumulated deficit of $260.9 million. Our net losses may fluctuate significantly from quarter to quarter and year to year. Although our expenses will decrease in conjunction with our restructuring and the decision to stop activities related to edasalonexent, we expect such decrease in costs to be offset, in part, by increased costs to initiate research, preclinical and clinical development efforts for QLS-215 and any other future product candidates; maintain, expand and protect our intellectual property portfolio; establish a commercial infrastructure to support the marketing and sale of QLS-215 and any other future product candidates; hire additional personnel, such as clinical, regulatory, quality control and scientific personnel; and operate as a public company.

At-the-Market Offerings

We have entered into various sales agreements with Cowen and Company LLC, or Cowen, pursuant to which we could issue and sell shares of our common stock under at-the-market, or ATM, programs. Cowen was not required to sell any specific amount but acted as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. Shares sold pursuant to these sales agreements were sold pursuant to shelf registration statements, one of which became effective on July 19, 2016, and which was replaced by a new shelf registration statement which became effective May 22, 2019. We have paid Cowen 3% of the gross proceeds from the common stock sold through these sales agreements.

During the year ended December 31, 2020, we sold an aggregate of 2,353,737 shares of common stock pursuant to our ATM programs, at an average offering price of $7.13 per share, for gross proceeds of $16.8 million, resulting in net proceeds of $16.3 million after deducting sales commissions and offering expenses. During the year ended December 31, 2019, we sold an aggregate of 1,282,904 shares of common stock pursuant to our ATM programs, at an average offering price of $5.81 per share, for gross proceeds of $7.5 million, resulting in net proceeds of $7.0 million after deducting sales commissions and offering expenses.

January 2020 Financing

On January 30, 2020, we entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of an aggregate of 5,290,000 shares of our common stock, at a price to the public of $5.00 per share, including 690,000 shares issued upon the exercise in full by Oppenheimer & Co. Inc. of its overallotment option. This resulted in gross proceeds of $26.5 million, and net proceeds of $24.6 million.

February 2019 Financing

On February 6, 2019, we entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of 4,000,000 shares of our common stock and accompanying warrants to purchase up to 2,000,000 shares of common stock, at a combined price to the public of $5.00 per unit, for gross proceeds of $20.0 million, and net proceeds of $18.5 million. The warrants were immediately exercisable at an exercise price of $6.25 per share and will expire five years from the date of issuance.

Funding Requirements

Our primary uses of capital are for compensation and related expenses, manufacturing costs for pre-clinical and clinical materials, third party pre-clinical research and development services, legal and other regulatory expenses and general overhead.

As of December 31, 2020, we had an accumulated deficit of $260.9 million. We have been primarily involved with research and development activities and have incurred operating losses and negative cash flows from operations since our inception.

As of December 31, 2020, we had available cash, cash equivalents and short-term investments of $44.9 million. Subsequent to December 31, 2020, we raised an additional $110.0 million in gross proceeds from the February 2021 Financing. We expect that our existing cash, cash equivalents and short-term investments, including the $110.0 million in gross proceeds from the February 2021 Financing, are sufficient to support our operating expenses through 2023, assuming our stockholders approve the conversion of the Series X Preferred Stock into common stock as discussed further below.

Our estimate as to how long we expect our cash, cash equivalents and short-term investments to be able to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including:

- our ability to integrate QLS-215 into our operations and meet our overall timing expectations for the program;
- the progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, QLS-215 any future product candidates, including potential future clinical trials;
- our ability to enter into and the terms and timing of any additional collaborations, licensing or other arrangements that we may establish;
- the number and characteristics of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, market access, distribution, supply chain and manufacturing capabilities, and scaling up the manufacturing of drug substance and drug product to clinical and commercial scale, securing all raw materials necessary to conduct such scale-up and successfully completing all other activities related thereto;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our product candidates;
- if we obtain marketing approval of any of our products, our ability to successfully compete against other approved products that are approved or used as treatments for the indications for which our products are approved, including with respect to QLS-215 in HAE;
- our headcount growth and associated costs;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the impact of the COVID-19 pandemic on our operations, business and prospects; and the costs of operating as a public company.

In connection with our acquisition of Quellis, we issued Series X Preferred Stock to Quellis stockholders in the Merger and to the Investors in the February 2021 Financing. We are obligated under the Merger Agreement to seek stockholder approval for the conversion of the Series X Preferred Stock into common stock. In the event that we fail to timely hold the stockholder meeting or fail to obtain stockholder approval, then the holders of the Series X Preferred Stock would be entitled to require us to redeem, in cash, the shares of common stock underlying their Series X Preferred Stock at a price per share equal to the fair value of the common stock. If we are forced to redeem a significant amount of shares underlying the Series X Preferred Stock, it could, among other things, materially affect our results of operations and cash usage forecasts, require us to slow down or stop the development of QLS-215 and any other future product candidates, require us to raise additional capital and impact our ability to raise additional capital. Also, while we cannot predict the amount with any level of certainty, there is a level of cash settlement at which, if it is exceeded, could require us to make redemption payments in excess of our current liquidity. Based on precedent transactions and the terms of the Series X Preferred Stock, we believe that our stockholders who are entitled to vote on the conversion proposal at our 2021 Annual Meeting of Stockholders, which is scheduled for June 2, 2021, will vote to approve the proposal. However, as the vote of our stockholders is outside of our control, there is substantial doubt about our ability to continue as a going concern within one year from the filing of this Annual Report on Form 10-K.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, QLS-215 or any future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would result in periodic payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

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

Cash Flows

Comparison of the Years Ended December 31, 2020 and 2019

The following table provides information regarding our cash flows for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Net cash used in operating activities	$(32,485)	$(26,569)
Net cash provided by (used in) investing activities	6,300	(4,082)
Net cash provided by financing activities	40,860	25,620
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 14,675	$ (5,031)

Net Cash Used in Operating Activities

Net cash used in operating activities was $32.5 million for the year ended December 31, 2020 and consisted primarily of a net loss of $37.3 million adjusted for non-cash items of $1.4 million, and a net decrease in operating assets of $3.4 million, which resulted primarily from a decrease in prepaid expenses and other current assets of $1.3 million and a decrease in the right of use asset of $0.2 million as well as increases in accrued expenses and accounts payable of $1.9 million.

Net cash used in operating activities was $26.6 million for the year ended December 31, 2019 and consisted primarily of a net loss of $26.3 million adjusted for non-cash items of $1.6 million, and a net increase in operating assets of $1.9 million, which resulted primarily from an increase in prepaid expenses and other current assets of $1.3 million, an increase in the right of use asset of $0.1 million as well as decreases in accounts payable, accrued expenses and other liabilities of $0.5 million.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $6.3 million for the year ended December 31, 2020 and consisted of proceeds from maturities of short-term investments of $69.1 million, which were partially offset by purchases of short-term investments of $62.8 million. Net cash used in investing activities was $4.1 million for the year ended December 31, 2019 and consisted primarily of purchases of short-term investments of $155.2 million partially offset by proceeds from maturities of short-term investments of $151.1 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $40.9 million during the year ended December 31, 2020, which was primarily attributable to net proceeds of $24.6 million from our January 2020 financing and net proceeds of $16.3 million from our ATM programs. Net cash provided by financing activities was $25.6 million during the year ended December 31, 2019, which was primarily attributable to net proceeds of $18.5 million from our February 2019 financing and net proceeds of $7.1 million from our ATM programs.

Off-Balance Sheet Arrangements

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

Contractual Obligations

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

	Payments due by period			
(In thousands)	Total	Less than 1 Year	1 – 3 Years	More than 3 Years
Operating lease obligations(1)	1,116	678	438	—
Total contractual cash obligations	$1,116	$678	$438	$—

(1) Represents future minimum lease payments under our non-cancelable operating lease. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

We enter into agreements in the normal course of business with vendors for preclinical research studies and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 60 days' prior written notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2020, we had cash, cash equivalents and short-term investments of $44.9 million and as of December 31, 2019, we had cash, cash equivalents and short-term investments of $36.2 million. Our cash equivalents as of December 31, 2020 consisted of money market funds and, as of December 31, 2019, consisted of corporate debt securities and money market funds. Our short-term investments as of December 31, 2020 consisted of United States reverse repurchase agreements and, as of December 31, 2019, consisted of commercial paper, corporate debt securities and United States reverse repurchase agreements. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio and interest income.

As of December 31, 2020 and December 31, 2019, we had no material liabilities that would require us to purchase foreign currency.

Item 8. Financial Statements and Supplementary Data

The consolidated financial statements together with the report of our independent registered public company accounting firm, required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those consolidated financial statements is found in Item 15 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2020, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Our 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. Our principal executive officer and principal financial officer

have concluded based upon the evaluation described above that, as of December 31, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

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

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control—Integrated Framework (2013). Based on its assessment, our management believes that, as of December 31, 2020, our internal control over financial reporting was effective based on those criteria.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting in accordance with an exemption established for smaller reporting companies with annual revenue of less than $100 million.

Changes in Internal Control over Financial Reporting

During the three months ended December 31, 2020, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is set forth under the captions "Proposal No. 1—Election of Class III Directors—Information Regarding Directors," "Corporate Governance," "Executive Officers," "Corporate Governance—Code of Business Conduct and Ethics" and "Compensation Governance—Committees of the Board of Directors—Audit Committee" in our definitive proxy statement for our 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2020, and is incorporated into this Annual Report on Form 10-K by reference.

We are also required under Item 405 of Regulation S-K to provide information concerning delinquent filers of reports under Section 16 of the Securities and Exchange Act of 1934, as amended. If applicable, this information will be set forth under the caption "Delinquent Section 16(a) Reports" in our definitive proxy statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC no later than 120 days after the end of our fiscal year and is incorporated herein by reference.

We have adopted a code of ethics, our Code of Business Conduct and Ethics, that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, and persons performing similar functions. Our Code of Business Conduct and Ethics, as well as our corporate governance guidelines and the charters for the audit, compensation, nominating and corporate governance, and science and technology committees of our Board of Directors, are each accessible under the "Corporate Governance" heading of the "Investors" section of our website, http://www.catabasis.com. We also intend to disclose in the same location on our website, any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation

The information required by this Item is set forth under the captions "Executive Officers," "Executive Compensation," and "Corporate Governance—Director Compensation" in our definitive proxy statement for our 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2020, and is incorporated into this Annual Report on Form 10-K by reference.

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

The information required by this Item is set forth under the captions "Securities Authorized for Issuance under Equity Compensation Plans" and "Principal Stockholders" in our definitive proxy statement for our 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2020, and is incorporated into this Annual Report on Form 10-K by reference

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

The information required by this Item is set forth under the captions "Corporate Governance—Director Independence" and "Certain Relationships and Related Person Transactions" in our definitive proxy statement for our 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2020 and is incorporated into this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item is set forth under the caption "Proposal No. 5—Ratification of the Appointment of Ernst & Young LLP as Catabasis' Independent Registered Public Accounting Firm for the Fiscal Year Ending December 31, 2021" in our definitive proxy statement for our 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2020 and is incorporated into this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements

The financial statements listed below are filed as part of this Annual Report on Form 10-K and are incorporated herein by reference.

(a)(2) Financial Statement Schedules

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements filed as part of this Annual Report on Form 10-K or the notes thereto or is not applicable or required.

(a)(3) Exhibits

The exhibits required for this Annual Report on Form 10-K by Item 601 of Regulation S-K and Item 15(b) of Form 10-K are listed in the following Exhibit Index:

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
2.1**	Agreement and Plan of Merger, dated January 28, 2021, by and among Catabasis Pharmaceuticals, Inc., Cabo Merger Sub I, Inc., Cabo Merger Sub II, LLC and Quellis Biosciences, Inc. (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on January 29, 2021)
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on July 1, 2015)
3.2	Certificate of Amendment to Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on December 31, 2018)
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on July 1, 2015)
3.4	Certificate of Designation of Series X Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on January 29, 2021)
4.1	Specimen stock certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on June 11, 2015)
4.2	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on June 20, 2018)
4.3	Form of Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on February 6, 2019)
4.4	Description of Registered Securities (incorporated by reference to Exhibit 4.4 to the Registrant's Annual Report on Form 10-K (File No. 001-37467) filed with the SEC on March 10, 2020)
10.1	Sales Agreement, dated May 14, 2019, by and between the Registrant and Cowen and Company, LLC (Incorporated by reference to Exhibit 1.1 to the Registrant's Registration Statement on Form S-3 (File No. 333-231441) filed with the SEC on May 14, 2019)
10.2+	Stock Purchase Agreement, dated as of January 28, 2021, by and among the Registrant and each purchaser identified on Annex A thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on January 29, 2021)
10.3+	Registration Rights Agreement, dated as of January 28, 2021, by and among the Registrant and each purchaser identified therein
10.4	Warrant to purchase shares of Series B Preferred Stock issued on August 27, 2014 by the Registrant to Square 1 Bank (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.5	Warrant to purchase shares of Series B Preferred Stock issued on August 27, 2014 by the Registrant to Midcap Financial SBIC, L.P. (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)

Exhibit Number	Description of Exhibit
10.6	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Square 1 Bank (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.7	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Midcap Financial Trust (incorporated by reference to Exhibit 10.20 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.8	Warrant to purchase shares of Series B Preferred Stock issued on March 31, 2015 to Flexpoint MCLS Holdings, LLC (incorporated by reference to Exhibit 10.21 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.9	Warrant to Purchase Shares of Series X Preferred Stock issued on January 28, 2021 to Viridian LLC
10.10	Warrant to Purchase Shares of Common Stock issued on January 28, 2021 to Viridian LLC
10.11*	Amended and Restated 2008 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.12*	Form of Incentive Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.13*	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.14*	Amended and Restated 2015 Stock Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Registration Statement on Form 8-K (File No. 001-37467) filed with the SEC on June 12, 2020)
10.15*	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on June 3, 2015)
10.16*	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on June 3, 2015)
10.17*	2015 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.22 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on June 3, 2015)
10.18*	Amended and Restated Employment Agreement, dated as of April 7, 2010, by and between the Registrant and Jill C. Milne, as amended (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)
10.19*	Amended and Restated Executive Severance Benefits Plan effective October 7, 2020 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on November 12, 2020)
10.20	Summary of Non-employee Director Compensation Program (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on May 12, 2016)
10.21*	Form of Indemnification Agreement by and between the Registrant and each of its executive officers and directors (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-204144) filed with the SEC on May 13, 2015)

Exhibit Number	Description of Exhibit
10.22	Sublease Agreement, dated as of September 14, 2018, by and between Inzen Therapeutics, Inc. and the Registrant (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-37467) filed with the SEC on October 16, 2018)
10.23	Sublease Agreement, dated as of September 9, 2019, by and between Allied Minds, LLC and the Registrant (Incorporated by reference to Exhibit 10.1 to the to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37467) filed with the SEC on November 7, 2019).
21.1	Subsidiaries of the Registrant
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
24.1	Power of Attorney (see signature page of this Annual Report on Form 10-K)
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Calculation Linkbase
101.LAB	XBRL Taxonomy Labels Linkbase Document
101.PRE	XBRL Taxonomy Presentation Linkbase Document
101.DEF	Taxonomy Extension Definition Linkbase Document

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* Management contract or compensatory plan arrangement.

** Exhibits and/or schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant hereby undertakes to furnish supplementally copies of any of the omitted exhibits and schedules upon request by the SEC; provided, however, that the Registrant may request confidential treatment pursuant to Rule 24b-2 of the Exchange Act for any exhibits or schedules so furnished. A list identifying the contents of all omitted exhibits and schedules can be found on page iii of Exhibit 2.1.

\+ Certain portions of this exhibit (indicated by "[***]") have been omitted because they are both (i) not material and (ii) would be competitively harmful if publicly disclosed.

Item 16. Form 10-K Summary

Not applicable

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of
Catabasis Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Catabasis Pharmaceuticals, Inc. (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2020, and 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 at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, in 2021 the Company issued preferred stock that could be redeemed by the holders for cash in excess of current liquidity if their convertibility to common stock is not approved by stockholders, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

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

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

Critical Audit Matter

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

Boston, Massachusetts

March 11, 2021

Catabasis Pharmaceuticals, 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	$ 24,930	$ 9,899
Short-term investments	20,000	26,345
Prepaid expenses and other current assets	1,395	2,714
Total current assets	46,325	38,958
Right-of-use asset	966	2,349
Other assets	165	473
Total assets	$ 47,456	$ 41,780
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,544	$ 1,197
Accrued expenses	4,197	2,610
Current portion of operating lease liabilities	649	1,225
Total current liabilities	6,390	5,032
Long-term portion of operating lease liabilities	397	1,028
Total liabilities	6,787	6,060
Commitments (Note 6)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share, 5,000,000 shares authorized and no shares issued and outstanding	—	—
Common stock, $0.001 par value per share, 150,000,000 shares authorized; 20,084,337 and 12,433,600 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	20	12
Additional paid-in capital	301,546	259,305
Accumulated other comprehensive loss	—	—
Accumulated deficit	(260,897)	(223,597)
Total stockholders' equity	40,669	35,720
Total liabilities and stockholders' equity	$ 47,456	$ 41,780

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

Catabasis Pharmaceuticals, Inc.

Consolidated Statements of Operations

(in thousands, except share and per share data)

	Year Ended December 31,	
	2020	**2019**
Operating expenses:		
Research and development	$ 25,590	$ 18,317
General and administrative	11,845	8,771
Total operating expenses	37,435	27,088
Loss from operations	(37,435)	(27,088)
Other income (expense):		
Interest and investment income	236	845
Other expense, net	(101)	(50)
Total other income, net	135	795
Net loss	$ (37,300)	$ (26,293)
Net loss per share—basic and diluted	$ (2.03)	$ (2.35)
Weighted-average common shares outstanding used in net loss per share—basic and diluted	18,351,470	11,199,057

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

Catabasis Pharmaceuticals, Inc.

Consolidated Statements Comprehensive Loss

(in thousands)

	Year Ended December 31,	
	2020	**2019**
Net loss	$(37,300)	$(26,293)
Other comprehensive income:		
Gain on short-term investments	—	4
Total other comprehensive income:	—	4
Comprehensive loss	$(37,300)	$(26,289)

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

Catabasis Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Gain	Total Stockholders' Equity
	Number of Shares	Par Value				
Balance at December 31, 2018	7,141,996	$ 7	$232,243	$(197,304)	$ (4)	$ 34,942
Issuance of common stock and warrants in public offering, net of $1.5 million in issuance costs	4,000,000	4	18,501	—	—	18,505
Issuance of common stock for at-the-market offerings, net of issuance costs of $0.4 million	1,282,904	1	6,995	—	—	6,996
Proceeds from exercises of warrants	8,700	—	54	—	—	54
Stock-based compensation expense	—	—	1,512	—	—	1,512
Unrealized gain on short-term investments	—	—	—	—	4	4
Net loss	—	—	—	(26,293)	—	(26,293)
Balance at December 31, 2019	12,433,600	$12	$259,305	$(223,597)	$—	$ 35,720
Issuance of common stock in public offering, net of $1.9 million in issuance costs	5,290,000	5	24,554	—	—	24,559
Issuance of common stock for at-the-market offerings, net of issuance costs of $0.5 million	2,353,737	3	16,267	—	—	16,270
Proceeds from exercises of options	7,000	—	31	—	—	31
Stock-based compensation expense	—	—	1,389	—	—	1,389
Net loss	—	—	—	(37,300)	—	(37,300)
Balance at December 31, 2020	20,084,337	$20	$301,546	$(260,897)	$—	$ 40,669

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

Catabasis Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2020	**2019**
Operating activities		
Net loss	$(37,300)	$ (26,293)
Reconciliation of net loss to net cash used in operating activities:		
Non-cash items	1,448	1,594
Changes in assets and liabilities:		
Prepaid expenses and other current assets	1,172	(1,289)
Other assets	85	—
Right-of-use asset- operating	176	(96)
Accounts payable	347	(211)
Accrued expenses	1,587	(205)
Other liabilities	—	(69)
Net cash used in operating activities	(32,485)	(26,569)
Investing activities		
Purchases of short-term investments	(62,777)	(155,197)
Sales and maturities of short-term investments	69,110	151,127
Purchases of property and equipment	(33)	(12)
Net cash provided by (used in) investing activities	6,300	(4,082)
Financing activities		
Proceeds from public offerings, net of issuance costs	24,559	18,505
Proceeds from at-the-market offering, net of issuance costs	16,270	7,061
Proceeds from exercise of common stock options and warrants	31	54
Net cash provided by financing activities	40,860	25,620
Net increase (decrease) in cash, cash equivalents and restricted cash	14,675	(5,031)
Cash, cash equivalents and restricted cash, beginning of period	10,376	15,407
Cash, cash equivalents and restricted cash, end of period	$ 25,051	$ 10,376
Non-cash financing activities:		
At-the-market offering issuance costs included in current liabilities	$ —	$ 65

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

1. Organization and Operations

The Company

Catabasis Pharmaceuticals, Inc (the "Company") is a biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics. Its mission is to bring hope with life-changing therapies to patients and families that are affected by rare diseases. On October 26, 2020, the Company announced that the Phase 3 PolarisDMD trial of the Company's previous lead product candidate, edasalonexent, for the treatment of Duchenne muscular dystrophy (DMD) did not meet its primary and secondary endpoints. Based on these results, the Company announced that it was stopping activities related to the development of edasalonexent, including the Company's ongoing open-label extension trial. On January 28, 2021, the Company acquired Quellis Biosciences, Inc ("Quellis"). The Company's lead product candidate, which was acquired in the Quellis acquisition, is QLS-215, a monoclonal antibody inhibitor of plasma kallikrein in preclinical development for the treatment of hereditary angioedema, or HAE, a rare, debilitating and potentially life-threatening disease. The Company was incorporated in the State of Delaware on June 26, 2008.

Liquidity

The Company has entered into various sales agreements with Cowen and Company LLC, ("Cowen"), pursuant to which the Company could issue and sell shares of common stock under at-the-market offering programs (the "ATM Programs"). Shares sold pursuant to these sales agreements were sold pursuant to shelf registration statements, one of which became effective on July 19, 2016 and which was replaced by a new shelf registration statement, which became effective May 22, 2019. The Company pays Cowen 3% of the gross proceeds from any common stock sold through these sales agreements. The Company currently has $27.9 million remaining available under its sales agreement.

During the year ended December 31, 2020, the Company sold an aggregate of 2,353,737 shares of common stock pursuant to the ATM Programs, at an average price of $7.13 per share, for gross proceeds of $16.8 million, resulting in net proceeds of $16.3 million after deducting sales commissions and offering expenses.

On January 30, 2020, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering (the "January 2020 Financing") of 5,290,000 shares of common stock at a price to the public of $5.00 per share. This resulted in gross proceeds of $26.5 million, and net proceeds of $24.6 million.

On February 6, 2019, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering (the "February 2019 Financing") of 4,000,000 shares of common stock and accompanying warrants to purchase up to 2,000,000 shares of common stock, at a combined price to the public of $5.00 per unit, for gross proceeds of $20.0 million and net proceeds of $18.5 million.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, successful discovery and development of its drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and regulatory approval and market acceptance of the Company's products. The Company has been primarily involved with research and development activities and has incurred operating losses and negative cash flows from operations since its inception. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop its product candidates.

As of December 31, 2020, the Company had an accumulated deficit of $260.9 million.The Company will require substantial additional capital to fund operations. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities. There can be no assurance that the Company will be able to obtain additional debt or

1. Organization and Operations (Continued)

equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations, and financial condition.

As of December 31, 2020, the Company had available cash, cash equivalents and short-term investments of $44.9 million. Subsequent to December 31, 2020, the Company raised gross proceeds of $110.0 million, and net proceeds of $104.0 million, through the February 2021 Financing (as described below). As part of the Quellis acquisition and the February 2021 Financing, the Company issued 86,077 shares of Series X Preferred Stock, which upon stockholder approval can be converted to 86,077,000 shares of common stock. The terms of the Series X Preferred Stock include a cash redemption feature. The redemption feature provides that, if the Company's common stockholders fail to approve the ability of the holders of the Series X Preferred Stock to convert their respective shares into common stock by July 28, 2021, the Company could, at the holder's option, be required to make a redemption payment to the holders of Series X Preferred Stock based on the then fair value of the Company's common stock underlying the redeemed Series X Preferred Stock significantly in excess of current liquidity. Based on precedent transactions and the terms of the Series X Preferred Stock, the Company believes that stockholders who are entitled to vote on the conversion proposal at the Company's 2021 Annual Meeting of Stockholders, which is scheduled for June 2, 2021, will vote to approve the proposal. However, as the vote of the Company's common stockholders is outside of the control of the Company, there is substantial doubt about its ability to continue as a going concern for at least 12 months following the issuance of these consolidated financial statements. The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Catabasis Securities Corporation. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from such estimates.

The Company utilizes certain estimates to record expenses relating to research and development contracts. These contract estimates, which are primarily related to the length of service of each contract and the amount of service provided as of each measurement date, are determined by the Company based on input from internal project management, as well as from third-party service providers.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign hedging arrangements. Financial instruments that subject the Company to credit risk primarily consist of cash, cash equivalents, short-term investments and restricted cash. The primary objectives for the Company's investment portfolio are the preservation of capital and the maintenance of liquidity. The

2. Summary of Significant Accounting Policies (Continued)

Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk.

Cash and Cash Equivalents and Restricted Cash

The Company considers highly liquid investments with a maturity of three months or less or reverse repurchase agreements with a maturity period of one business day or less when purchased to be cash equivalents. Cash equivalents, which consist of money market funds, corporate debt securities and reverse repurchase agreements are stated at fair value. Cash and cash equivalents consist of the following (in thousands):

	December 31,	
	2020	2019
Cash	$ 1,931	$2,530
Money market fund	22,999	5,432
Corporate debt securities	—	1,937
Total	$24,930	$9,899

The reconciliation of cash, cash equivalents and restricted cash reported within the applicable balance sheet that sum to the total of the same such amount shown in the statement of cash flows is as follows (in thousands):

	December 31,	
	2020	2019
Cash and cash equivalents	$24,930	$ 9,899
Restricted cash(1)	121	477
Total	$25,051	$10,376

(1) Included in prepaid expenses and other current assets and other assets.

Short-Term Investments

The Company classifies all corporate debt securities with a remaining maturity of greater than three months and reverse repurchase agreements with a remaining maturity of greater than one business day at the time of purchase as short-term investments. Short-term investments are recorded at fair value, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, interest, dividends and declines in value judged to be other-than-temporary are included in interest and investment income.

The cost of securities sold is based on the specific identification method for purposes of recording realized gains and losses. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary.

Fair Value of Financial Instruments

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical

2. Summary of Significant Accounting Policies (Continued)

assets or liabilities; Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The carrying amounts reflected in the balance sheets for cash equivalents, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at December 31, 2020 and 2019, due to their short-term nature. There have been no changes to the valuation methods during the years ended December 31, 2020 and 2019. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between levels during the year ended December 31, 2020 and 2019.

The Company's investment portfolio may include fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. The Company validates the prices provided by its third party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances. The Company also invests in certain reverse repurchase agreements which are collateralized by deposits in the form of United States Government Securities and Obligations for an amount no less than 102% of their value. The Company does not record an asset or liability for the collateral as the Company is not permitted to sell or re-pledge the collateral. The collateral has at least the prevailing credit rating of United States Government Treasuries and Agencies. The Company utilizes a third party custodian to manage the exchange of funds and ensure that collateral received is maintained at 102% of the value of the reverse repurchase agreements on a daily basis.

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any significant impairment charges from inception through December 31, 2020.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs include salaries and personnel-related costs, stock-based compensation, consulting fees, fees paid for contract research services, the costs of laboratory equipment and facilities and other external costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred. The deferred amounts are expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with Accounting Standards Codification ("ASC") Topic 718, *Compensation—Stock Compensation (*"ASC 718"). ASC 718 requires all share-based payments to employees, including grants of employee stock options, to be recognized in the statements of operations based on their grant date fair values. For granted stock options, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the Company's common stock consistent with the expected term of the option, risk-free interest rates and expected dividend yields of the Company's common stock.

2. Summary of Significant Accounting Policies (Continued)

For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period.

The Company expenses restricted stock awards based on the fair value of the award on a straight-line basis over the associated service period of the award.

During the years ended December 31, 2020 and 2019, the Company recorded stock-based compensation expense for employee and non-employee stock options and restricted stock, which was allocated as follows in the statements of operations (in thousands):

	Year Ended December 31,	
	2020	2019
Research and development	$ 599	$ 616
General and administrative	790	896
Total	$1,389	$1,512

No related tax benefits were recognized for the years ended December 31, 2020 and 2019.

Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the Company's dilutive net loss per share calculation, stock options and warrants to purchase the Company's common stock were considered to be common stock equivalents but were excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2020	2019
Stock options	1,367,667	785,832
Common stock warrants	6,193,749	6,193,749
	7,561,416	6,979,581

Income Taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more likely than not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC Topic 740, *Expenses—Income Taxes*. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax

2. Summary of Significant Accounting Policies (Continued)

position as well as consideration of the available facts and circumstances. The Company did not have any significant uncertain tax positions for any periods presented.

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker, the Company's chief executive officer, in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business in one operating segment. The Company operates in one geographic segment.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the year ended December 31, 2019 the amount in accumulated other comprehensive loss were comprised of unrealized gains and losses on short-term investments.

Leases

Effective January 1, 2019, the Company determines if an arrangement is a lease at inception. Operating leases are included in right-of-use ("ROU") lease assets, current portion of lease obligations, and long-term lease obligations on the Company's balance sheets. The Company does not currently hold any financing leases.

ROU lease assets represent the Company's right to use an underlying asset for the lease term and lease obligations represent the Company's obligation to make lease payments arising from the lease. Operating ROU lease assets and obligations are recognized at the commencement date based on the present value of lease payments over the lease term. As the Company's facility leases do not provide an implicit rate, the Company uses its estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The Company's ROU lease assets also include any lease payments made and excludes lease incentives. If the Company's facility lease includes options to terminate the lease which would affect the lease period when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments under facility leases are recognized on a straight-line basis over the lease term.

Recent Accounting Pronouncements—Adopted

In August 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") 2018-13, *Fair Value Measurement (Topic 820)*. This standard includes amendments regarding changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and disclosure requirements of measurement uncertainty. This amendment was effective for annual reporting periods beginning after December 15, 2019. Adoption of the standard did not have a material impact on the Company's consolidated financial statements.

Recent Accounting Pronouncements—Not Yet Adopted

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

2. Summary of Significant Accounting Policies (Continued)

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses* (Topic 326). This standard requires a financial asset to be presented at amortized cost basis at the net amount expected to be collected. It also requires that credit losses relating to available-for-sale debt securities should be recorded through an allowance for credit losses. In November 2019, the FASB issued an amendment making this ASU effective for annual reporting periods beginning after December 15, 2022 for smaller reporting companies. Early adoption is permitted. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements as well as the timing of when this standard will be adopted.

3. Financial Instruments

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value, and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value. Below is a summary of assets and liabilities measured at fair value on a recurring basis (in thousands):

	As of December 31, 2020			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$22,999	$ —	$—	$22,999
Short-term investments:				
Reverse repurchase agreements	—	20,000	—	20,000
Total assets	$22,999	$20,000	$—	$42,999

	As of December 31, 2019			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Cash and cash equivalents:				
Money market funds	$5,432	$ —	$—	$ 5,432
Corporate debt securities	—	1,937	—	1,937
Short-term investments:				
Commercial paper	—	1,993	—	1,993
Corporate debt securities	—	3,352	—	3,352
Reverse repurchase agreements	—	21,000	—	21,000
Total assets	$5,432	$28,282	$—	$33,714

4. Short-Term Investments

The following table summarizes the short-term investments held at December 31, 2020 and 2019 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2020				
Reverse repurchase agreements	$20,000	$—	$—	$20,000
Total	$20,000	$—	$—	$20,000

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2019				
Commercial paper	$ 1,993	$—	$—	$ 1,993
Corporate debt securities	3,352	—	—	3,352
Reverse repurchase agreements	21,000	—	—	21,000
Total	$26,345	$—	$—	$26,345

The contractual maturities of all short-term investments held at December 31, 2020 and 2019 were one year or less. There were no short-term investments in an unrealized loss position at December 31, 2020. There were four short-term investments in an unrealized loss position at December 31, 2019, none of which had been in an unrealized loss position for more than 12 months. The aggregate fair value of these securities at December 31, 2019 was approximately $3.4 million. The Company did not hold any securities with other-than-temporary impairments at December 31, 2020 and 2019.

Gross realized gains and losses on the sales of short-term investments are included in other income, net. Unrealized holding gains or losses for the period that have been included in accumulated other comprehensive income, as well as gains and losses reclassified out of accumulated other comprehensive income into other income, net were not material to the Company's consolidated results of operations. During the years ended December 31, 2020 and 2019 all proceeds included in the Company's cash flows related to maturities of underlying securities. The gains on proceeds of maturities of short-term investments were not material to the Company's consolidated results of operations for the years ended December 31, 2020 and 2019.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Accrued contracted research costs	$1,726	$ 737
Accrued compensation	1,719	1,365
Accrued severance	396	—
Accrued professional fees	356	370
Accrued other	—	138
Total	$4,197	$2,610

6. Commitments

In November 2019, the Company entered into a sublease for office space which was classified as an operating lease. At inception of the lease, the Company recognized a lease liability and right-of-use asset of approximately $1.7 million. The lease liability represents the present value of the remaining lease payments, discounted using the Company's estimated incremental borrowing rate of 7.49%. The ROU asset represents the lease liability adjusted for any prepaid and accrued rent payments.

Future minimum payments required under the non-cancelable operating leases as of December 31, 2020 are summarized as follows (in thousands):

Period Ending December 31,	Amount
2021	678
2022	438
Total lease payments	$1,116
Less: imputed interest	(70)
Total operating lease liabilities	$1,046

Rent expense was $0.8 million and $0.4 million for the years ended December 31, 2020 and 2019, respectively. Lease payments were $1.5 million and $1.4 million for the years ended December 31, 2020 and 2019, respectively.

7. Stockholders' Equity

Preferred Stock

As of December 31, 2020, the Company had 5,000,000 shares of preferred stock authorized for issuance, $0.001 par value per share, with none issued or outstanding. Preferred stock may be issued from time to time in one or more series, each series to have such terms as stated or expressed in the resolutions providing for the issue of such series adopted by the board of directors of the Company. Preferred stock which may be redeemed, purchased or acquired by the Company may be reissued except as otherwise provided by law.

Common Stock Warrants

February 2019 Warrants

In the February 2019 Financing, the Company issued warrants to purchase 2,000,000 shares of common stock with an exercise price of $6.25 per share, which were immediately exercisable upon issuance and expire in February 2024.

The terms of the warrants include certain provisions related to fundamental transactions, a cashless exercise provision in the event registered shares are not available, and do not include any mandatory redemption provisions. Therefore, the warrants have been classified in stockholders' equity. Any changes to the fair value of the warrants will not be recognized so long as the warrants continue to be equity classified.

As of December 31, 2020, warrants to purchase 1,991,300 shares that were issued in the February 2019 Financing were outstanding with a remaining contractual life of 3.1 years.

June 2018 Warrants

On June 19, 2018, the Company entered into an underwriting agreement with Oppenheimer & Co. Inc. relating to an underwritten public offering of 4,200,000 shares of the Company's common stock, par value

7. Stockholders' Equity (Continued)

$0.001 per share, and accompanying warrants to purchase up to 4,200,000 shares of common stock. The warrants have an exercise price of $12.00 per share, were immediately exercisable upon issuance and expire in June 2023.

The terms of the warrants include certain provisions related to fundamental transactions, a cashless exercise provision in the event registered shares are not available and do not include any mandatory redemption provisions. Therefore, the warrants have been classified in stockholders' equity. Any changes to fair value of the warrants will not be recognized so long as the warrants continue to be equity classified.

As of December 31, 2020, all warrants related to this transaction were outstanding with a remaining contractual life of 2.5 years.

Common Stock

As of December 31, 2020, the Company had 150,000,000 shares of common stock authorized for issuance, $0.001 par value per share, with 20,084,337 shares issued and outstanding. The voting, dividend and liquidation rights of holders of common stock are subject to and qualified by the rights, powers and preferences of the holders of any outstanding preferred stock.

Reserved for Future Issuance

The Company has reserved for future issuance the following shares of common stock:

	December 31, 2020	December 31, 2019
Warrants for the purchase of common stock	6,193,749	6,193,749
Options outstanding to purchase common stock	1,367,667	785,832
Options available for future issuance to purchase common stock	1,936,173	525,484
Shares reserved for the employee stock purchase plan	148,951	112,481
Total	9,646,540	7,617,546

8. Stock Incentive Plans

Prior to the Company's initial public offering in June 2015 (the "IPO"), the Company granted awards to eligible participants under its 2008 Equity Incentive Plan. In May 2015, the Company's board of directors adopted and, in June 2015, the Company's stockholders approved the 2015 Stock Incentive Plan ("2015 Plan"), which became effective immediately prior to the effectiveness of the IPO. Subsequent to the IPO, option grants are awarded to eligible participants only under the 2015 Plan.

The 2015 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2015 Plan.

Terms of stock option agreements, including vesting requirements, are determined by the Company's board of directors, subject to the provisions of the applicable stock incentive plan. Options granted by the Company generally vest ratably over four years, with a one-year cliff, and options are exercisable from the date of grant for a period of ten years. For options granted through December 31, 2020, the exercise price or purchase price, as applicable, equaled the estimated fair value of the common stock as determined by the Company's board of directors on the date of grant.

8. Stock Incentive Plans (Continued)

A summary of the Company's stock option activity and related information for employees and non-employees follows:

	Shares	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2019	785,832	$16.48	8.13	$470
Granted	666,200	$ 5.69		
Exercised	(7,000)	$ 4.39		
Cancelled or forfeited	(76,884)	$14.65		
Expired	(481)	$32.10		
Outstanding at December 31, 2020	1,367,667	$11.38	8.13	$ —
Vested and exercisable at December 31, 2020	504,171	$21.22	6.68	$ —

The total intrinsic value of options exercised in the year ended December 31, 2020 was $29 thousand. There were no options exercised in the year ended December 31, 2019. The weighted-average grant date fair value of options granted to employees and non-employees for the years ended December 31, 2020 and 2019 was $3.81 and $3.25, respectively.

At December 31, 2020, the total unrecognized compensation expense related to unvested stock option awards was $2.7 million. The Company expects to recognize that cost over a weighted-average period of approximately 2.7 years.

Stock-Based Compensation Expense

The fair value of stock options granted to employees and non-employees was estimated using the Black-Scholes option-pricing model based on the following assumptions:

	Year Ended December 31,	
	2020	2019
Weighted-average expected volatility	75.51 - 82.08%	68.9 - 110.5%
Expected term (in years)	5.50 - 6.25	5.50 - 10.00
Risk-free interest rate	0.37 - 1.51%	1.39 - 2.69%
Expected dividend yield	0%	0%

Volatility

Due to the lack of company-specific historical and implied volatility data of its common stock, the Company does not have relevant historical data to support its expected volatility. As such, the Company has used a weighted average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as number of product candidates in early stages of product development, area of therapeutic focus, and length of trading history. The expected volatility was determined using an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to continue to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

8. Stock Incentive Plans (Continued)

Expected Term

The Company uses the "simplified method" to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's share-based awards.

Risk-Free Rate

The risk-free rate was based on the yield curve of United States Treasury securities with periods commensurate with the expected term of the options being valued.

9. Income Taxes

For the years ended December 31, 2020 and 2019, the Company did not record a provision for federal or state income taxes as it has incurred cumulative net operating losses since inception.

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
Federal income tax (benefit) at statutory rate	21.00%	21.00%
Permanent differences	(0.41)	(0.57)
Federal research and development credits and adjustments	2.78	2.42
State income tax, net of federal benefit	6.03	5.50
Other	0.37	0.49
Change in valuation allowance	(29.77)	(28.85)
Effective income tax rate	—%	—%

The Company's deferred tax assets consisted of the following (in thousands):

	Year Ended December 31,	
	2020	2019
Deferred tax assets		
Net operating loss carryforwards	$ 65,373	$ 55,283
Tax credit carryforwards	9,273	8,030
Capitalized research and development	482	922
Capitalized legal expenses	1,070	1,073
Lease liability	284	639
Other differences	1,648	1,453
Total deferred tax assets	78,130	67,400
Deferred tax liabilities		
ROU asset	(262)	(639)
Valuation allowance	(77,868)	(66,761)
Net deferred tax assets	$ —	$ —

The Company recorded an increase to the valuation allowance of $11.1 million during the year ended December 31, 2020 due primarily to the federal and state net operating losses and tax credits generated. The

9. Income Taxes (Continued)

Company recorded an increase to the valuation allowance of $7.6 million during the year ended December 31, 2019 which was also primarily due to the federal and state net operating losses and tax credits generated.

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company's history of losses and expectation of future losses, the deferred tax assets were fully offset by a valuation allowance at December 31, 2020 and 2019.

As of December 31, 2020, the Company had approximately $240.1 million of federal and $236.7 million of state net operating loss respectively, which may be available to offset future taxable income. Federal net operating loss carryforwards of $150.5 million and state net operating loss carryforwards of $236.7 million will expire at various dates from 2023 through 2040. Federal net operating loss carryforwards of $89.6 can be carried forward indefinitely. The Company had approximately $7.4 million of federal and $2.4 million of state tax credit carryforwards available to reduce future tax liabilities as of December 31, 2020, which will expire at varying times through the year 2040.

The Internal Revenue Code of 1986, as amended (the "Code"), provides for a limitation of the annual use of net operating losses and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the Code) that could limit the Company's ability to utilize these carryforwards. At this time, the Company has not completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since the Company's formation, due to the costs and complexities associated with such a study. The Company may have experienced various ownership changes, as defined by the Code, as a result of past financing transactions. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes. Therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security (CARES) Act was signed into law making several changes to the Internal Revenue Code. The changes include, but are not limited to: increasing the limitation on the amount of deductible interest expense, allowing companies to carryback certain net operating losses, and increasing the amount of net operating loss carryforwards that corporations can use to offset taxable income. The tax law changes in the Act did not have a material impact on the Company's income tax provision.

As of December 31, 2020 and 2019, the Company did not have any significant unrecognized tax benefits. The Company had not accrued interest or penalties related to uncertain tax positions.

The federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2017 through December 31, 2020. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state taxing authorities to the extent utilized in a future period.

10. Defined Contribution Benefit Plan

The Company sponsors a 401(k) retirement plan, in which substantially all of its employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company did not provide any contributions to this plan during the years ended December 31, 2020 or 2018.

11. Subsequent Events

Agreement and Plan of Merger

On January 28, 2021, the Company acquired Quellis. Under the terms of the Merger Agreement, the Company issued to the stockholders of Quellis 3,332,669 shares of the Company's common stock, par value $0.001 per share, and 50,504 shares of newly designated Series X Preferred Stock (as described below) which had a conversion value on the closing date of $122.7 million. In addition, the Company assumed options granted under the Quellis stock option plan, a warrant to purchase 2,805 shares of Series X Preferred Stock at an exercise price of $341.70 per share, and a warrant to purchase 185,136 shares of the Company's common stock at an exercise price of $0.35 per share, which warrants are exercisable until December 14, 2030.

Stock Purchase Agreement

On January 28, 2021, the Company entered into a Stock Purchase Agreement (the "Purchase Agreement") with certain institutional and accredited investors (the "Investors"). Pursuant to the Purchase Agreement, the Company agreed to sell an aggregate of 35,573 shares of Series X Preferred Stock for gross proceeds of approximately $110.0 million (the "February 2021 Financing").

Series X Preferred Stock

As a result of the above transactions, in 2021 the Company issued the following Series X Preferred Stock or warrants to purchase Series X Preferred Stock:

	Series X Preferred Shares	Common Stock Issuable Upon Conversion[1]
Outstanding shares issued in merger	50,504	50,504,000
Outstanding shares issued in February 2021 Financing	35,573	35,573,000
Warrants assumed in merger	2,805	2,805,000
Total	88,882	88,882,000

(1) Requires stockholder approval for conversion.

Subject to stockholder approval, each share of Series X Preferred Stock is convertible into 1,000 shares of common stock.

The Company is required to hold a stockholders' meeting to submit the following matters to its stockholders for their consideration: (i) the approval of the conversion of the Series X Preferred Stock into shares of the Company's common stock in accordance with Nasdaq Listing Rule 5635(a) (the "Conversion Proposal") and (ii) if necessary or appropriate, the approval of an amendment to the certificate of incorporation of the Company to authorize sufficient shares of common stock for the conversion of the Series X Preferred Stock issued pursuant to the Merger Agreement and the Purchase Agreement (as described above) and/or to effectuate a reverse stock split, the "Charter Amendment Proposal."

If the Company's stockholders do not approve the conversion of the Series X Preferred Stock by July 28, 2021, then the holders of the Series X Preferred Stock are entitled to require the Company to make redemption payments at a price per share equal to the fair value of undelivered shares of common stock, defined as the last reported closing price of the Company's common stock on the trading day on which notice of conversion is delivered to the Company. Using the closing price on March 4, 2021 of $2.87, if all currently outstanding Series X Preferred Stock was redeemed for cash, the Company would be required to make a payment of $247.0 million. The Company has insufficient liquidity to make such a payment, if required.

11. Subsequent Events (Continued)

Holders of Series X Preferred Stock are entitled to receive dividends on shares of Series X Preferred Stock equal, on an as-if-converted-to-common-stock basis, and in the same form as dividends actually paid on shares of the Company's common stock. Except as otherwise required by law, the Series X Preferred Stock does not have voting rights. However, as long as any shares of Series X Preferred Stock are outstanding, the Company may not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series X Preferred Stock, (i) alter or change adversely the powers, preferences or rights given to the Series X Preferred Stock or alter or amend the Certificate of Designation that authorized the Series X Preferred Stock, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series X Preferred Stock, (ii) issue further shares of Series X Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series X Preferred Stock, or (iii) enter into any agreement with respect to any of the foregoing. Additionally, the approval of the holders of a majority of the Series X Preferred Stock is required for certain change of control transactions, provided that this approval right will terminate upon stockholder approval of the Conversion Proposal.

Following stockholder approval of the Conversion Proposal, on the fourth business day after the date on which such stockholder approval is received, each share of Series X Preferred Stock then outstanding automatically converts into 1,000 shares of the Company's common stock, subject to certain beneficial ownership limitations, including that a holder of Series X Preferred Stock is prohibited from converting shares of Series X Preferred Stock into shares of the Company's common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (to be initially set at 9.99% and thereafter adjustable by the holder to a number between 4.99% and 19.99%) of the total number of shares of the Company's common stock issued and outstanding immediately after giving effect to such conversion. Shares of Series X Preferred Stock not converted automatically are thereafter subject to conversion at the option of the holder.

Registration Rights Agreement

On January 28, 2021, the Company entered into a Registration Rights Agreement (the "Registration Rights Agreement") with the Investors. Pursuant to the Registration Rights Agreement, the Company agreed to prepare and file a resale registration statement with the SEC within 90 calendar days following the closing of the February 2021 Financing (the "Filing Deadline"). The Company agreed to use its reasonable best efforts to cause this registration statement to be declared effective by the SEC within 30 calendar days of the Filing Deadline (or within 60 calendar days if the SEC reviews the registration statement).

The Company also agreed, among other things, to indemnify the Investors, their officers, directors, members, employees and agents, successors and assigns under the registration statement from certain liabilities and pay all fees and expenses (excluding any legal fees of the selling holder(s), and any underwriting discounts and selling commissions) incident to the Company's obligations under the Registration Rights Agreement.

SIGNATURES

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

Catabasis Pharmaceuticals, Inc.

Date: March 11, 2021

By: /s/ JILL C. MILNE
Jill C. Milne
President and Chief Executive Officer

We, the undersigned directors and officers of Catabasis Pharmaceuticals, Inc. (the "Company"), hereby severally constitute and appoint Jill C. Milne and Noah Clauser, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

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

Signature	Title	Date
/s/ JILL C. MILNE Jill C. Milne	President and Chief Executive Officer and Director(Principal Executive Officer)	March 11, 2021
/s/ NOAH CLAUSER Noah Clauser	Chief Financial Officer and Treasurer (Principal Financial Officer, Principal Accounting Officer)	March 11, 2021
/s/ KENNETH BATE Kenneth Bate	Chairman	March 11, 2021
/s/ JOANNE BECK Joanne Beck	Director	March 11, 2021
/s/ FREDERICK C. CALLORI Frederick C. Callori	Director	March 11, 2021
/s/ HUGH COLE Hugh Cole	Director	March 11, 2021
/s/ MICHAEL KISHBAUCH Michael Kishbauch	Director	March 11, 2021

Signature	Title	Date
/s/ Gregg Lapointe Gregg Lapointe	Director	March 11, 2021
/s/ Jonathan Violin Jonathan Violin	Director	March 11, 2021

Directors and Executive Officers (as of April 16, 2021)

Directors	*Executive Officers*
Kenneth Bate, Chair of the Board of Directors of Catabasis Pharmaceuticals, Inc.	**Jill Milne**, Chief Executive Officer and President
Joanne Beck, Chief Operations Officer, Boston Pharmaceuticals	**Noah Clauser**, Chief Financial Officer
Fred Callori, Senior Vice President, Corporate Development, Xontogeny, LLC, and partner, Perceptive Xontogeny Venture Fund	**Joanne Donovan**, Chief Medical Officer[(1)]
Hugh Cole, Chief Business Officer and Head of Corporate Development, Jounce Therapeutics	**Benjamin Harshbarger**, General Counsel
Michael Kishbauch, Former President and Chief Executive Officer, Achillion Pharmaceuticals	**Andrew Komjathy**, Chief Commercial Officer
Gregg Lapointe, Co-Founder and Chief Executive Officer, Cerium Pharmaceuticals, Inc.	**Andrew Nichols**, Chief Scientific Officer
Jill Milne, Chief Executive Officer and President, Catabasis Pharmaceuticals, Inc.	
Jonathan Violin, President and Chief Executive Officer, Viridian Therapeutics, Inc.	

(1) Dr. Donovan resigned as our Chief Medical Officer effective April 23, 2021.

Stockholder Information Requests

Stockholders who desire information about Catabasis Pharmaceuticals, Inc. may contact us at 100 High Street, 28th Floor, Boston, MA 02110 (telephone: 617-349-1971; email: investors@catabasis.com). Information of interest to stockholders and investors, such as our annual reports, quarterly reports, proxy statements, press releases and other information, is available on our website at www.catabasis.com under "investors."

Stock Transfer Agent

American Stock Transfer & Trust Company (AST) is the stock transfer agent for our common stock and maintains common stockholder activity records. AST will respond to questions on issuance of common stock certificates, change of ownership, lost common stock certificates and change of address. For these and similar matters, please direct inquiries to: American Stock Transfer and Trust Company, Shareholder Services Department, 6201 15th Avenue, Brooklyn, NY 11219 (telephone: 718-921-8214 or 800-937-5449) or visit www.amstock.com.

2021 Virtual Annual Meeting

Our 2021 Annual Meeting of Stockholders is scheduled to be held exclusively online via the internet as a virtual web conference at www.virtualshareholdermeeting.com/CATB2021 on Wednesday, June 2, 2021 at 9:00 a.m. Eastern Time.

Forward Looking Statements

This annual report contains forward-looking statements within the meaning of applicable federal securities laws and regulations. Any statements contained in this annual report that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "believes," intends," "anticipates," "plans," "expects," "seeks," "estimates," "would," "should," "likely," "will," "may," "continue," "could," or similar expressions are intended to identify forward-looking statements. While we may elect to update forward-looking statements in the future, we specifically disclaim any obligation to do so, even if our expectations change. A number of factors could cause our results to differ materially from those indicated by such forward-looking statements, including those detailed under the heading "Risk Factors" in Part 1, Item 1A in the accompanying Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and our subsequent filings with the U.S. Securities and Exchange Commission.