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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): February 10, 2021

Kadmon Holdings, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-37841**	**27-3576929**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

450 East 29th Street
New York, NY **10016**
(Address of principal executive offices) **(Zip Code)**

Registrant's telephone number, including area code (833) 900-5366

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company x

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. x

ITEM 2.02 Results of Operations and Financial Condition

The information contained in Exhibit 99.2 of this Current Report on Form 8-K (the "Current Report") under the heading "Expected Full-Year 2020 Results" furnishes specified preliminary expectations with respect to the financial results of Kadmon Holdings, Inc. (the "Company") for the full-year ended December 31, 2020 and is incorporated into this Item 2.02 by reference.

The information furnished under this Item 2.02 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly set forth by specific reference in such a filing.

ITEM 8.01 Other Events

On February 10, 2021, the Company issued a press release (the "Press Release") announcing its intention to offer, subject to market and other conditions, convertible senior notes due 2027 in an aggregate principal amount of $150,000,000 in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended (the "Offering"). A copy of the Press Release is filed as Exhibit 99.1 hereto and is incorporated into this Item 8.01 by reference.

In addition, the information contained in Exhibit 99.2 of this Current Report under the heading "Risk Factors" contains an update of the Company's risk factor disclosure and is incorporated into this Item 8.01 by reference.

ITEM 9.01 Financial Statements and Exhibits

(d) Exhibits.

Exhibit No.	**Description**
99.1	Press Release dated February 10, 2021
99.2	Disclosure Update as of February 10, 2021
104	Cover Page Interactive Data (embedded within Inline XBRL document)

SIGNATURE

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

Kadmon Holdings, Inc.

Date: February 10, 2021

/s/ Harlan W. Waksal
Harlan W. Waksal, M.D.
President and Chief Executive Officer

Kadmon Announces Proposed $150 Million Convertible Senior Notes Offering with Capped Call Transactions

NEW YORK, February 10, 2021 – Kadmon Holdings, Inc. (Nasdaq: KDMN) today announced its intent to offer, subject to market conditions and other factors, $150 million aggregate principal amount of convertible senior notes due 2027 (the "Notes") in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended. Kadmon also expects to grant the initial purchaser of the Notes a 13-day option to purchase up to an additional $30 million aggregate principal amount of the Notes, solely to cover over-allotments.

The Notes will mature on February 15, 2027, unless earlier converted, redeemed or repurchased and will be convertible, subject to the satisfaction of certain conditions, into cash, shares of Kadmon common stock or a combination thereof as elected by Kadmon in its sole discretion. The Notes will be general unsecured obligations of Kadmon and interest will be payable semi-annually in arrears. Kadmon will have the right to redeem the Notes on or after February 20, 2024, subject to certain conditions. Final terms of the Notes, including the initial conversion rate, interest rate and other terms, will be determined upon pricing of the offering.

In connection with the pricing of the Notes, Kadmon expects to enter into capped call transactions with one or more financial institutions (the "option counterparties"). The capped call transactions will cover, subject to customary adjustments, the number of shares of common stock initially underlying the Notes. The capped call transactions are expected to generally reduce the potential dilutive effect on Kadmon's common stock upon conversion of the Notes or at Kadmon's election (subject to certain conditions) offset any cash payments Kadmon is required to make in excess of the aggregate principal amount of converted Notes, with such reduction and/or offset subject to a cap.

In connection with establishing their initial hedges of the capped call transactions, the option counterparties or their respective affiliates expect to enter into various derivative transactions with respect to Kadmon's common stock and/or purchase shares of Kadmon's common stock concurrently with or shortly after the pricing of the Notes (and, if applicable, the exercise by the initial purchaser of its over-allotment option). This activity could increase (or reduce the size of any decrease in) the market price of Kadmon's common stock or the Notes at that time. In addition, the option counterparties or their respective affiliates may modify their hedge positions by entering into or unwinding various derivatives with respect to Kadmon's common stock and/or purchasing or selling Kadmon's common stock or other securities issued by Kadmon in secondary market transactions following the pricing of the Notes and prior to the maturity of the Notes (and are likely to do so on each exercise date of the capped call transactions, which are expected to occur during the 40 trading day period beginning on the 41st scheduled trading day prior to the maturity date of the Notes, or following any early termination of any portion of the capped call transactions in connection with any repurchase, redemption or early conversion of the Notes). This activity could also cause or avoid an increase or a decrease in the market price of Kadmon's common stock or the Notes, which could affect

a noteholder's ability to convert the Notes and, to the extent the activity occurs during any observation period related to a conversion of the Notes, it could affect the number of shares and value of the consideration that a noteholder will receive upon conversion of the Notes.

In addition, if any capped call transaction fails to become effective, whether or not this offering of the Notes is completed, the option counterparties party thereto may unwind their hedge positions with respect to Kadmon's common stock, which could adversely affect the value of Kadmon's common stock and, if the Notes have been issued, the value of the Notes.

Kadmon intends to use a portion of the proceeds to prepare to commercialize belumosudil in chronic graft-versus-host disease in the United States, if approved; for the development of its other clinical-stage product candidates; for the discovery, research and preclinical studies of its other product candidates; and other general corporate purposes. Kadmon intends to use the balance of the net proceeds from the offering to fund the cost of entering into the capped call transactions described above. In addition, if the initial purchaser exercises its over-allotment option, then Kadmon intends to use a portion of the additional net proceeds for general corporate purposes as described above and to fund the cost of entering into the capped call transactions.

This press release does not constitute an offer to sell or the solicitation of an offer to buy any securities of Kadmon. Any offers of the Notes will be made only by means of a private offering memorandum. The offer and sale of the Notes and any shares of Kadmon common stock issuable upon conversion of the Notes have not been, and will not be, registered under the Securities Act or the securities laws of any other jurisdiction, and the Notes and such shares may not be offered or sold in the United States absent registration or an applicable exemption from the Securities Act and applicable state laws.

About Kadmon

Kadmon is a clinical-stage biopharmaceutical company that discovers, develops and delivers transformative therapies for unmet medical needs. Kadmon's clinical pipeline includes treatments for immune and fibrotic diseases as well as immuno-oncology therapies.

Forward Looking Statements

This press release contains forward-looking statements. Such statements may be preceded by the words "may," "will," "should," "expects," "plans," "anticipates," "could," "intends," "targets," "projects," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. These forward-looking statements include, without limitation, statements regarding the completion, timing and size of the proposed offering, the intended use of the proceeds, the terms of the Notes being offered, the anticipated terms of, and the effects of entering into, the capped call transactions described above and the actions of the option counterparties and their respective affiliates. Forward-looking statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Among those risks and uncertainties are risks related to market conditions, including market interest rates, and the trading price and volatility of Kadmon's common stock. We believe that these factors also include, but are not limited to, (i) the initiation, timing, progress and results of our preclinical studies and clinical

trials, and our research and development programs; (ii) our ability to advance product candidates into, and successfully complete, clinical trials; (iii) the impact of the COVID-19 pandemic on our business, workforce, patients, collaborators and suppliers, including delays in anticipated timelines and milestones of our clinical trials and on various government agencies who we interact with and/or are governed by; (iv) our reliance on the success of our product candidates; (v) the timing or likelihood of regulatory filings and approvals, including the acceptance of our NDA for belumosudil, especially in light of the COVID-19 pandemic; (vi) our ability to expand our sales and marketing capabilities; (vii) our ability to expand our sales and marketing capabilities; (viii) the commercialization, pricing and reimbursement of our product candidates, if approved; (ix) the implementation of our business model, strategic plans for our business, product candidates and technology; (x) the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology; (xi) our ability to operate our business without infringing the intellectual property rights and proprietary technology of third parties; (xii) costs associated with defending intellectual property infringement, product liability and other claims; (xiii) regulatory developments in the United States, Europe, and other jurisdictions; (xiv) estimates of our expenses, future revenues, capital requirements and our needs for additional financing; (xv) the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements; (xvi) our ability to maintain and establish collaborations; (xvii) the rate and degree of market acceptance of our product candidates, if approved; (xviii) developments relating to our competitors and our industry, including competing therapies; (xix) our ability to effectively manage our anticipated growth; (xx) our ability to attract and retain qualified employees and key personnel; (xxi) our expected use of cash and cash equivalents and other sources of liquidity; (xxii) the potential benefits of any of our product candidates being granted orphan drug designation; (xxiii) the future trading price of the shares of our common stock and impact of securities analysts' reports on these prices; (xxiv) our ability to apply unused federal and state net operating loss carryforwards against future taxable income and/or (xv) other risks and uncertainties. More detailed information about the Company and the risk factors that may affect the realization of forward-looking statements is set forth in the Company's filings with the U.S. Securities and Exchange Commission (the "SEC"), including Kadmon's Annual Report on Form 10-K for the fiscal year ended December 31, 2019. Investors and security holders are urged to read these documents free of charge on the SEC's website at www.sec.gov. The Company assumes no obligation to publicly update or revise its forward-looking statements as a result of new information, future events or otherwise.

Contact Information
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Kadmon Holdings, Inc. Disclosure Update as of February 10, 2021

As used in this Exhibit 99.2, unless the context indicates otherwise, references to "Kadmon," "the Company," "we," "us," "our" and similar references refer to Kadmon Holdings, Inc. and its wholly owned subsidiaries.

Special note regarding forward-looking statements

This document contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this document may be forward-looking statements. Statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, including, among others, statements regarding future expenditures, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expects," "plans," "anticipates," "could," "intends," "targets," "projects," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions.

Forward-looking statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. We believe that these factors include, but are not limited to, the following:

- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the impact of the COVID-19 pandemic on our business, workforce, patients, collaborators and suppliers, including delays in anticipated timelines and milestones of our clinical trials and on various government agencies who we interact with and/or are governed by;
- our reliance on the success of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the benefits of U.S. Food and Drug Administration designations such as Breakthrough Therapy, and review of our New Drug Application under the FDA's Oncology Center of Excellence (OCE) pilot program, Real-Time Oncology Review (RTOR), and the FDA's Project Orbis initiative (Project Orbis);
- the commercialization, pricing and reimbursement of our product candidates, if approved, and our ability to expand our sales and marketing capabilities;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology and our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights and proprietary technology of third parties;
- cost associated with defending or enforcing, if any, intellectual property infringement, misappropriation or other intellectual property violation, product liability and other claims;
- regulatory and governmental policy developments in the United States, Europe and other jurisdictions;

- our ability to maintain and establish strategic agreements and collaborations and the potential benefits of those arrangements;
- the rate and degree of market acceptance, if any, of our product candidates, if approved;
- developments relating to our competitors and our industry, including competing therapies;
- our ability to effectively manage our anticipated growth;
- our ability to attract and retain qualified employees and key personnel;
- our ability to achieve cost savings and benefits from our efforts to streamline our operations and to not harm our business with such efforts;
- our expectations regarding the period during which we qualify as an emerging growth company under the Jumpstart Our Business Startups Act;
- statements and estimates regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements, needs for additional financing and share performance;
- litigation, including costs associated with prosecuting or defending pending or threatened claims and any adverse outcomes or settlements not covered by insurance;
- our expected use of cash, cash equivalents and marketable debt securities and other sources of liquidity;
- the future trading price of the shares of our common stock and the impact of analysts' reports on these prices;
- our ability to apply unused federal and state net operating loss carryforwards against future taxable income; and/or
- other risks and uncertainties, including those listed under the caption "Risk factors" in this Exhibit 99.2 of the Current Report on Form 8-K of which this document is a part.

While we believe that we have a reasonable basis for each forward- looking statement, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many of these risks, uncertainties and other factors are discussed in greater detail in in Exhibit 99.2 of the Current Report on Form 8-K of which this document is a part. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. We hereby qualify all forward-looking statements by these cautionary statements. We claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 for all forward-looking statements.

Except as required by law, we do not assume any obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

Expected Full-year 2020 Results

Our financial results for the full year are not yet finalized. However, we are providing the following information reflecting our preliminary expectations with respect to its financial results as of and for the year ended December 31, 2020 based on currently available information:

For the year ended December 31, 2020:

- Revenues are expected to be approximately $8.3 million; and
- Net loss is expected to be approximately $108.9 million.

At December 31, 2020:

- Cash and cash equivalents, together with marketable debt securities, are expected to equal $123.9 million; and
- Accumulated deficit is expected to be approximately $444.1 million.

Our audited consolidated financial statements for the year ended December 31, 2020 are not yet available. Accordingly, the year-end financial results presented above are preliminary, unaudited, and subject to the completion of our financial closing procedures and should not be viewed as a substitute for full-year financial statements prepared in accordance with generally accepted accounting principles. As a result, these preliminary

results may differ from the actual results that will be reflected in our consolidated financial statements for the period when they are completed and publicly disclosed.

Our expectations with respect to its unaudited results for the period presented above reflect management's estimates based solely upon information available to it as of the date of this Current Report. The Company's independent registered public accounting firm, BDO USA, LLP, has not audited, reviewed or performed any procedures with respect to these preliminary results and, accordingly, does not express an opinion or any other form of assurance about them. An audit, review or set of procedures of such financial information could result in changes to these preliminary results. Actual results may be materially different from the preliminary expectations, and undue reliance should not be placed on these current expectations.

Risk Factors

An investment in our securities involves a high degree of risk. You should carefully consider the following risk factors. The risks and uncertainties described in these documents are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment.

Risks related to our financial position and need for capital

We are a clinical stage biopharmaceutical company with a history of operating losses.

We are a clinical stage pharmaceutical company with a history of operating losses. We must complete clinical studies and receive regulatory approval before commercial sales of a product can commence. The likelihood of success of our business plan must be considered in light of the problems, substantial expenses, difficulties, complications and delays frequently encountered in connection with developing and expanding early-stage businesses and the regulatory and competitive environment in which we operate. Pharmaceutical product development is a highly speculative undertaking, involves a substantial degree of risk and is a capital-intensive business.

Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical pharmaceutical companies such as ours. Potential investors should carefully consider the risks and uncertainties that a company with a limited operating history will face. In particular, potential investors should consider that we cannot assure you that we will be able to:

- successfully implement or execute our current business plan, and we cannot assure you that our business plan is sound;
- successfully manufacture our clinical products and establish commercial drug supply;
- successfully complete the clinical trials necessary to obtain regulatory approval for the marketing of our product candidates;
- secure market exclusivity and/or adequate intellectual property protection for our product candidates;
- attract and retain an experienced management and advisory team;
- secure acceptance of our product candidates in the medical community and with third party payors and consumers;
- launch commercial sales of our product candidates, whether alone or in collaboration with others; and
- raise sufficient funds in the capital markets to effectuate our business plan.

If we cannot successfully execute any one of the foregoing, our business may not succeed and your investment will be adversely affected.

We have incurred substantial losses since our inception. We may not achieve or sustain profitability. These factors individually and collectively raise a substantial doubt about or ability to continue as a going concern.

Since inception, we have incurred substantial operating losses. Our consolidated net losses are expected to be $108.9 million for the year ended December 31, 2020 and were $61.4 million for the year ended December 31,

2019. Our accumulated deficits are expected to be approximately $444.1 million at December 31, 2020 and were $333.1 million at December 31, 2019. To date, we have financed our clinical development operations primarily through issuance of common stock and other equity securities in public and private offerings and debt financings. We expect to continue to incur significant expenses related to the development of our clinical product candidates for at least the next several years. We anticipate that our expenses will increase substantially as we:

- initiate or continue our clinical trials related to our most advanced product candidates;
- continue the research and development of our other product candidates;
- seek to discover additional product candidates;
- seek regulatory approvals for our product candidates;
- scale up our sales, marketing and distribution infrastructure and product sourcing capabilities to commercialize additional products we may acquire or license from others or for which we may develop and obtain regulatory approval; and/or
- scale up our operational, financial and management information systems and personnel, including personnel to support our product development and planned additional commercialization efforts.

In the absence of substantial revenue from the sale of our products and products that we distribute, or from other sources (the amount, timing, nature or source of which cannot be predicted), we expect our substantial losses to continue as we develop our business and we may need to discontinue operations. Our ability to generate sufficient revenues from our existing products or from any of our product candidates in development, and to transition to profitability and generate consistent positive cash flow is uncertain. We may continue to incur losses and negative cash flow and may never transition to profitability or positive cash flow and, as a result, there is substantial doubt over our ability to continue as a going concern.

Our independent registered public accounting firm has included an explanatory paragraph in its report as of and for the year ended December 31, 2019 expressing substantial doubt in our ability to continue as a going concern based on our recurring and continuing losses from operations and our need for additional funding to continue operations. Our consolidated financial statements as of December 31, 2019 do not include any adjustments that might result from the outcome of this going concern uncertainty and have been prepared under the assumption that we will continue to operate as a going concern for the next twelve months, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. If we are unable to continue as a going concern we may be forced to liquidate our assets which would have an adverse impact on our business and developmental activities. In such a scenario, the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements. The reaction of investors to the inclusion of a going concern statement by our independent registered public accounting firm and our potential inability to continue as a going concern may materially adversely affect our stock price and our ability to raise new capital or to enter into strategic alliances.

We will need additional funding in the future, which may not be available to us, and this may force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We will need to expend substantial resources for research and development and commercialization of our marketed products, including costs associated with:

- clinical trials for our product candidates;
- discovery of additional product candidates;
- life-cycle management of our marketed products;
- the continued commercialization of our commercial products; and/or
- preparing for potential commercialization of our late-stage product candidates and, if one or more of those product candidates receive(s) regulatory approval, to fund the launch of that (those) product(s).

We do not expect that our existing cash, cash equivalents and restricted cash will be sufficient to enable us to fund the completion of development and commercialization of any of our product candidates. We do not have any additional committed external source of funds. Our expenses may increase for many reasons, including:

- clinical trial-related expenses for our product candidates;
- the potential launch and marketing of our late-stage product candidates; and/or

- manufacturing scale-up for commercialization of our late-stage product candidates.

To the extent that we need to raise additional capital through the sale of equity or convertible debt securities, investors in our common stock will be diluted, and the terms of any newly issued securities may include liquidation or other preferences that adversely affect the value of our common stock.

Risks related to our clinical development pipeline

We depend heavily on the success of belumosudil. If we are unable to obtain regulatory approval for belumosudil, our ability to create near-term stockholder value will be limited.

Our most advanced product candidate is belumosudil (KD025), for which we have submitted applications for regulatory approval in the US and in several other jurisdictions under Project Orbis. We do not generate meaningful revenues from any FDA-approved drug products. Three of our product candidates, belumosudil, KD033 and tesevatinib, are in clinical trials and we have additional internally developed product candidates, which are in the early stages of development. There is no guarantee that our clinical trials will be successful or that we will continue with clinical studies to support an approval from the FDA of any of our product candidates for any indication. We note that most drug candidates never reach the clinical development stage and even those that do have only a small chance of successfully completing clinical development and gaining regulatory approval. Therefore, our business currently depends heavily on the successful development, regulatory approval and commercialization of belumosudil, which may never occur.

Clinical development is a lengthy and expensive process with a potentially uncertain outcome. Our long-term success depends upon the successful development and commercialization of our product candidates, which is highly uncertain.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early clinical trials may not be predictive of the results of later-stage clinical trials. We cannot assure you that the FDA will view the results as we do or that any future trials of our drug candidates will achieve positive results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Any future clinical trial results for our drug candidates may not be successful.

In addition, a number of factors could contribute to a lack of favorable safety and efficacy results for our drug candidates. For example, such trials could result in increased variability due to varying site characteristics, such as local standards of care, differences in evaluation period and surgical technique, and due to varying patient characteristics, including demographic factors and health status.

To date, we have invested a significant portion of our efforts and financial resources in the acquisition and development of our product candidates. Our long-term success depends upon the successful development, regulatory approval and commercialization of these product candidates. If we fail to obtain regulatory approval to market and sell our product candidates, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased. Our business depends significantly on the successful development, regulatory approval and commercialization of our product candidates, which may never occur.

We cannot be certain as to what type and how many clinical trials the FDA will require us to conduct before we may successfully gain approval to market any of our product candidates. Prior to approving a new drug or biologic, the FDA generally requires that the effectiveness of the product candidate (which is not typically fully investigated until Phase 3) be demonstrated in two adequate and well-controlled clinical trials. In some situations, the FDA approves drugs or biologics on the basis of a single well-controlled clinical trial establishing effectiveness. However, if the FDA determines that our Phase 3 clinical trial results do not demonstrate a statistically significant, clinically significant benefit with an acceptable safety profile, or if the FDA requires us to conduct additional Phase 3 clinical trials in order to gain approval, we will incur significant additional development costs and commercialization of these products would be prevented or delayed and our business would be adversely affected.

Our ongoing clinical trials may be subject to delays or setbacks for a variety of common and unpredictable reasons.

We may experience unforeseen delays or setbacks in our ongoing clinical trials, such as trial initiation timing, trial redesign or amendments, timing and availability of patient enrollment or successful trial completion. Such delays and setbacks are common and unpredictable in pharmaceutical drug development. Clinical trials can be delayed for a variety of reasons, including delays related to:

- regulatory objections to commencing a clinical trial, continuing a clinical trial that is underway, or proceeding to the next phase of investigation, including inability to reach agreement with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials or for other reasons such as safety concerns that might be identified through preclinical testing and animal studies or clinical trials, at any stage;
- reaching agreement on acceptable terms with prospective contract research organizations (CROs), and clinical trial sites (the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites);
- failure of CROs or other third-party contractors to comply with contractual and regulatory requirements or to perform their services in a timely or acceptable manner;
- difficulty identifying and engaging qualified clinical investigators;
- obtaining institutional review board (IRB) approval at each site;
- difficulty recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indication as product candidates we seek to commercialize;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- inability to retain patients in clinical trials due to the treatment protocol, personal issues, side effects from the therapy or lack of efficacy, particularly for those patients receiving a placebo;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- adding new clinical trial sites;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our product candidates;
- changes in applicable regulatory policies and regulations;
- insufficient data to support regulatory approval;
- difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data; or
- manufacturing sufficient quantities of the product candidate for use in clinical trials.

In late 2019, a novel strain of COVID-19, also known as coronavirus, was reported in Wuhan, China and began spreading to various parts of the world. Epidemics have adversely impacted, and may adversely impact in the future, our business as they can cause disruptions, such as interruptions to supply chain and reduction in access to personnel and services, which could result in delays and complications with respect to our research and development programs and clinical trials. In addition, certain of our business partners and vendors are based in areas currently affected by coronavirus, which could cause additional adverse impact on our business.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including:

- failure by us, CROs or clinical investigators to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- failed inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety or efficacy issues or any determination that a clinical trial presents unacceptable health risks;
- failure to demonstrate a benefit from using a drug; or
- lack of adequate funding to continue the clinical trial due to unforeseen costs resulting from enrollment delays, requirements to conduct additional trials and studies, increased expenses associated with the services of our CROs and other third parties, changes in governmental regulations or administrative actions, or other reasons.

If we experience delays in the completion or termination of any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

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

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support a submission for regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and/or
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may:

- approve any of our product candidates for fewer or more limited indications than we request;
- may not approve the price we intend to charge for our products;
- may grant approval contingent on the performance of costly post-marketing clinical trials; or
- may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

If we do not achieve our projected development goals in the timeframes we announce and expect, or we face significant competition from other biotechnology and pharmaceutical companies, the commercialization of our products may be delayed, our operating results may be lower that we expect, the credibility of our management may be adversely affected and, as a result, the value of our common stock may decline.

Breakthrough Therapy Designation, priority review of our NDA for belumosudil under the FDA's RTOR pilot program and our marketing applications in other jurisdictions pursuant to the FDA's Project Orbis initiative, may not lead to a faster regulatory review or approval, and do not increase the likelihood that belumosudil will obtain marketing approval.

Belumosudil has received "breakthrough therapy" designation by the FDA. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies may also be eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. In addition, the FDA or other regulatory bodies periodically introduce pilot programs with the goal of a more efficient review of applications, including the RTOR pilot program, which is currently being tested by the FDA. The RTOR pilot program allows the FDA to review data before the applicant formally submits its completed application, aiming to explore a more efficient review process. The FDA's Project Orbis is an initiative of the FDA Oncology Center of Excellence (OCE) and, according to the FDA, is designed to provide a framework for concurrent submission and review of oncology products among international partners.

The Company has submitted applications for marketing approval in several jurisdictions pursuant to project Orbis. According to the FDA, Project Orbis provides a framework for concurrent submission and review of

oncology products among international partners. Participation in the RTOR and Project Orbis pilot programs does not guarantee or influence approvability of our marketing applications for belumosudil in certain patients with cGVHD, which are subject to the applicable review standards of the respective regulatory agencies, and we may not derive any benefit from inclusion in these programs, including, but not limited to, a more efficient review process. These programs are not formal regulatory pathways and may be changed, suspended, or halted at any time. Priority review is an FDA designation under which the FDA sets the target date for FDA action on a NDA at six months after the FDA accepts the application for filing, rather than the standard 10-month FDA review period. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition.

Although Breakthrough Therapy Designation, priority review designation, the RTOR pilot program and Project Orbis initiative, and other designations we may receive or programs we may participate in, are intended to expedite the review and approval of drug candidates, they do not ensure that marketing approval will be granted in a particular timeframe, or at all. The FDA and other regulatory authorities have broad discretion whether or not to grant designations for expedited review or include product candidates within various programs, and, even if we or our partners believe a particular product candidate is eligible for these designations or programs, we cannot assure you that such authority would agree. Even though the FDA has granted priority review designation for our NDA for belumosudil, and even if we or our partners receive such designations or our product candidates are eligible for inclusion in expedited review programs in the future, we may not experience a faster development, review, or approval process compared to conventional procedures. Furthermore, these designations and programs do not change the scientific and medical standard for approval or the quality of evidence necessary to support approval. As a result, applications for product candidates granted priority review or other expedited review designations or subject to these various programs may be denied based on study data, study design, or other factors.

Even if we obtain regulatory approval for our product candidates, they may never be successfully launched or become profitable, in which case our business, prospects, operating results and financial condition may be materially harmed.

In order to successfully launch our product candidates and have them become profitable, we anticipate that we will have to dedicate substantial time and resources and hire additional personnel to expand and enhance our commercial infrastructure, which will at a minimum include the following:

- ensure the quality of the product candidate manufactured by our suppliers and by us;
- expand our sales and marketing force;
- expand and enhance programs and other procedures to educate physicians and drive physician adoption of our product candidates;
- create additional policies and procedures, and hire additional personnel to carry out those policies and procedures, to ensure customer satisfaction with our products;
- obtain reimbursement for hospitals and physicians; and/or
- expand and enhance our general and administrative operations to manage our anticipated growth in operations and to support public company activities.

Because of the numerous risks and uncertainties associated with launch and profitability of our product candidates, we are unable to predict the extent of any future losses, or when we will become profitable, if ever.

If serious adverse events or other undesirable side effects are identified during the use of product candidates in investigator-sponsored trials, it may adversely affect our development of such product candidates.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt non-clinical studies and clinical trials, or could make it more difficult for us to enroll patients in our clinical trials. If serious adverse events or other undesirable side effects, or unexpected characteristics of our product candidates are observed in investigator-sponsored trials, further clinical development of such product candidate may be delayed or we may not be able to continue development of such product candidate at all, and the occurrence of these events could have a material adverse effect on our business. Undesirable side effects caused by our product candidates could also result in the delay or denial of regulatory approval by the FDA or other regulatory authorities or in a more restrictive label than we expect.

Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is obtained, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Undesirable or unexpected side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval and we or others later identify undesirable or unexpected side effects caused by such products, a number of potentially significant negative consequences could result, including:

- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly; and/or
- our reputation may suffer.

In addition, a regulatory agency may:

- suspend or withdraw approvals of such product;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us, our collaborators or our potential future collaborators;
- require additional warnings on the label;
- require that we create a medication guide outlining the risks of such side effects for distribution to patients;
- issue warning letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us or our collaborators to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other civil or criminal penalties;
- impose restrictions on operations, including costly new manufacturing requirements; and/or
- seize or detain products or require a product recall.

Non-compliance may also result in potential whistleblower lawsuits and the potential for liability under the False Claims Act or other laws and regulations, as discussed above. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.

Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any of our current and future collaborators may decide, or regulators may require us, to conduct additional clinical or preclinical testing. In addition, data obtained from tests are susceptible to varying interpretations, and regulators may not interpret data as favorably as we do, which may delay, limit or prevent regulatory approval.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that future larger registration clinical trials will

be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through initial clinical trials. Product candidates that have shown promising results in early clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Similarly, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

Further, at various points during the course of the preclinical and clinical trial process, companies must assess both the statistical and clinical significance of trial results. In this context, "statistical significance" refers to the likelihood that a result or relationship is caused by something other than random chance or error. Statistical significance is measured by a "p-value," which indicates the probability value that the results observed in a study were due to chance alone. A p-value of < 0.05 is generally considered statistically significant, meaning that the probability of the results occurring by chance alone is less than five percent. The lower the p-value, the less likely that the results observed were random. "Clinical significance," on the other hand, is a qualitative assessment of the results observed. Where we use the term "clinically significant," we have not necessarily made a formal statistical assessment of the probability that the change in patient status was attributable to the study drug as opposed to chance alone, nor does such a statement necessarily mean that study endpoints have been met or the protocol has been completed. A clinically significant effect is one that is determined to have practical importance for patients and physicians, and includes benefits that are often defined by peer-reviewed literature as having a meaningful impact on a patient's condition. An effect that is statistically significant may or may not also be clinically significant. When a study fails to result in statistical significance, the FDA may not consider such study to serve as substantial evidence of safety and effectiveness required for approval. Even if a study results in statistical significance, the FDA may also consider clinical significance in evaluating a marketing application. For example, the FDA typically requires more than one pivotal clinical study to support approval of a new drug. However, the FDA has indicated that approval may be based on a single study in limited situations in which a trial has demonstrated a clinically significant effect. In either case, the clinical or statistical significance of a particular study result in no way guarantees that FDA or other regulators will ultimately determine that the drug being investigated is safe and effective.

In addition, 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 may be unable to design and execute a clinical trial to support regulatory approval.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 1, Phase 2, Phase 3 or other clinical trials we or any of our collaborators may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

Further, our product candidates may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or registration trials. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in the FDA or other agencies' approval. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

We face substantial competition, which may result in others discovering, developing and commercializing products before or more successfully than our products and product candidates.

The development and commercialization of new therapeutics is highly competitive. We face competition (from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide) with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or products we commercialize in the future. We also face competition from

academic research institutions, governmental agencies and other various public and private research institutions. Many of these competitors are attempting to develop therapeutics for our target indications. With the proliferation of new drugs and therapies in these areas, we expect to face increasingly intense competition as new technologies become available. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are products already approved for many of the diseases we are targeting. Many of these approved products are well established therapies and are widely accepted by physicians, patients and third-party payors. This may make it difficult for us to achieve our business strategy of replacing existing therapies with our product candidates. Our commercial operations face significant direct competition and our competitors may develop products that are safer, more effective, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic 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.

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

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

Risks related to our marketed products

Even if we receive regulatory approval for our drug candidates, we cannot be certain how profitable, if at all, the commercialization of our marketed products will be.

We must compete effectively against other therapies with our products or any of our product candidates for which we obtain marketing approval. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability.

In addition to the risks discussed elsewhere in this section, our ability to continue to generate revenues from our commercialized products will depend on a number of factors, including, but not limited to:

- achievement of broad market acceptance and coverage by third-party payors for our products;
- the effectiveness of our collaborators' efforts in marketing and selling our products;
- our ability to successfully manufacture, or have manufactured, commercial quantities of our products at acceptable cost levels and in compliance with regulatory requirements;
- our ability to maintain a cost-efficient organization and, to the extent we seek to do so, to collaborate successfully with additional third parties;
- our ability to expand and maintain intellectual property protection for our products successfully;
- the efficacy and safety of our products; and/or
- our ability to comply with regulatory requirements, which are subject to change.

Because of the numerous risks and uncertainties associated with our commercialization efforts, we may not be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. A failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our inability to accurately estimate demand for our products, the uptake of new products or the timing of fluctuations in the inventories maintained by customers makes it difficult for us to accurately forecast sales and may cause our financial results to fluctuate.

We may be unable to accurately estimate demand for our products, including uptake from new products, as demand is dependent on a number of factors. We sell products primarily to wholesalers and specialty pharmacies. These customers maintain and control their own inventory levels by making estimates to determine end user demand. Our customers may not be effective in matching their inventory levels to actual end user demand. As a result, changes in inventory levels held by our customers can cause our operating results to fluctuate unexpectedly. Adverse changes in economic conditions or other factors may cause our customers to reduce their inventories of our products, which would reduce their orders from us, even if end user demand has not changed. If our inventory exceeds demand from our customers and exceeds its shelf life, we will be required to destroy unsold inventory and write off its value. As our inventory and distribution channels fluctuate from quarter to quarter, we may continue to see fluctuations in our earnings and a mismatch between prescription demand for our products and our revenues.

If we discover safety issues with any of our products or if we fail to comply with continuing U.S. and applicable foreign regulations, commercialization efforts for the product could be negatively affected, the approved product could be subject to withdrawal of approval or sales could be suspended, and our business could be materially harmed.

Our products are subject to continuing regulatory oversight, including the review of additional safety information. Drugs are more widely used by patients once approval has been obtained and therefore side effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre-approval clinical trials or nonclinical studies. The subsequent discovery of previously unknown problems with a product, or public speculation about adverse safety events, could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market.

If we or our collaborators fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals for specific products, product recalls and seizures, injunctions, consent decrees or other operating restrictions and/or criminal prosecutions. In addition, the manufacturers we engage to make our products and the manufacturing facilities in which our products are made are subject to periodic review and inspection by the FDA and foreign regulatory authorities. If problems are identified during the review or inspection of these manufacturers or manufacturing facilities, it could result in our inability to use the facility to make our product or a determination that inventories are not safe for commercial sale.

Failure to comply with FDA promotional rules may subject us to withdrawal, and correction, of related product promotion, seizure of product and other administrative or enforcement actions as well as the potential for ancillary liability under the False Claims Act and/or product liability litigation.

The FDA regulates the promotion of our products, which may only be promoted within their approved indication for use. Promotional materials and activity must be presented with fair balance of the risks and benefits of any product in a manner which is not otherwise inaccurate or misleading. The FDCA and the FDA's implementing regulations require that manufacturers label, advertise and promote their products with appropriate safety warnings and adequate directions for their FDA-approved use. However, the FDA does not have the legal authority to regulate the practice of medicine. Although physicians are permitted, based on their medical judgment, to prescribe products for indications other than those approved by the FDA, manufacturers are prohibited from promoting their products for such off-label uses.

If the FDA determines that our promotional materials, training or other activities constitute off-label promotion, it could request that we modify our training or promotional materials or other activities or subject us to regulatory enforcement actions, including the issuance of a warning letter, injunction, seizure, civil fine and criminal penalties. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and

advertising of prescription drugs may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. The FDA or other regulatory authorities could also request that we enter into a consent decree or a corporate integrity agreement, or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed.

Although recent decisions of the United States Supreme Court, the U.S. Court of Appeals for the Second Circuit and the U.S. District Court for the Southern District of New York have clarified that the United States may not, consistent with the First Amendment, restrict or punish a pharmaceutical manufacturer's truthful and non-misleading speech promoting the lawful use of an approved drug, there are still significant risks in this area. It is unclear how these court decisions will impact the FDA's enforcement practices, and there is likely to be substantial disagreement and difference of opinion regarding whether any particular statement is truthful and not misleading.

In the past we have been subject to enforcement action relating to allegations of improper promotion of our products, and we may be subject to such action in the future.

If we cannot successfully manage the promotion of our currently marketed products, and product candidates, if approved, we could become subject to significant liability which would materially adversely affect our business and financial condition. It is also possible that other federal, state or foreign enforcement authorities, or private parties, might take action if they believe that an alleged improper promotion led to inappropriate use of one of our products and/or the submission and payment of claims for an off-label use, which could result in significant fines or penalties under other statutory provisions, such as the False Claims Act and similar laws. Even if it is later determined that we were not in violation of these laws, we may face negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters. In addition, there are a number of specific FDA requirements related to drug labeling and advertising, and failure to adhere to these requirements could result in our products being deemed "misbranded."

The manufacture of pharmaceutical products is a highly complex process, and if our suppliers encounter problems manufacturing our products, our business could suffer.

The manufacture of pharmaceutical products is a highly complex process, due in part to strict regulatory requirements. Problems may arise during manufacturing for a variety of reasons, including equipment malfunction, failure to follow specific protocols and procedures, problems with raw materials, delays related to the construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products, changes in manufacturing production sites and limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, physical limitations that could inhibit continuous supply, man-made or natural disasters and environmental factors. If problems arise during the production of a batch of product, that batch of product may have to be discarded and we may experience product shortages or incur added expenses. This could, among other things, lead to increased costs, lost revenue, damage to customer relationships, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred.

Risks related to government regulation

If we engage in research or commercial activities involving any of our products or pipeline assets in a manner that violates federal or state healthcare laws, including fraud and abuse laws, false claims laws, disclosure laws, government price reporting and healthcare information privacy and security laws or other similar laws, we may be subject to corporate or individual civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business operations and activities are subject to extensive federal, state and local fraud and abuse and other healthcare laws and regulations, such as the False Claims Act and the federal Anti-Kickback Statute, the Foreign Corrupt Practices Act ("FCPA"), federal Physician Payment Sunshine Act, the federal Drug Supply Chain Security Act, federal Civil Monetary Penalty statute, the PPACA program integrity requirements, patient privacy laws and regulation, criminal laws relating to healthcare fraud and abuse, including but not limited to the Health Insurance Portability and Accountability Act, federal consumer protection and unfair competition laws, federal government price reporting laws and state law equivalents of each of these. These laws and regulations constrain, among other things, the business or financial arrangements and relationships through which we may research and develop any product candidate, as well as market, sell and distribute any approved products.

In addition, any sales of our products or product candidates, if approved, commercialized outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

We have entered into consulting agreements, scientific advisory board and other financial arrangements with physicians, including some who prescribe our products and may prescribe our product candidates, if approved. Compensation for some of these arrangements includes the provision of stock options. While these arrangements were structured to comply with all applicable laws, including state and federal anti-kickback laws, to the extent applicable, regulatory agencies may view these arrangements as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant penalties. Moreover, while we do not submit claims and our customers make the ultimate decision on how to submit claims, we may provide reimbursement guidance and support to our customers and patients. If a government authority were to conclude that we provided improper advice to our customers and/or encouraged the submission of false claims for reimbursement, we could face action against by government authorities.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. The sales and marketing practices of our industry are the subject of immense scrutiny from federal and state government agencies. Despite sequestration measures, governmental enforcement funding continues at robust levels and enforcement officials are interpreting fraud and abuse laws broadly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are subject to a variety of interpretations. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources, divert our management's attention from the operation of the business, and generate negative publicity, which could harm our business. If our past or present operations are found to be in violation of any such laws or any other governmental regulations that may apply to us, we may be subject to, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and/or the curtailment or restructuring of our operations.

Our commercial success depends on adequate reimbursement and coverage from third-party commercial and government payors for our products, and changes to coverage or reimbursement policies, as well as healthcare reform measures, may materially harm our sales and potential revenue.

Most patients rely on reimbursement from third-party payors, including government programs (such as Medicare and Medicaid) and private payor healthcare and insurance programs to pay for their medical needs, including any drugs we may market. Coverage and reimbursement for our products can differ significantly from

payor to payor. Even when we obtain coverage and reimbursement for our products, we may not be able to maintain adequate coverage and reimbursement in the future.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved products. We intend to seek approval to market our product candidates in the United States, Europe and other selected foreign jurisdictions. Market acceptance and commercial success of our product candidates in both domestic and international markets will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for any of our product candidates.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. Additionally, coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside of the United States. Assuming that coverage is obtained for a given product, the resulting reimbursement rates might not be adequate or may require co-payments that patients find unacceptably high. Patients, physicians, and other healthcare providers may be less likely to prescribe, dispense or use, as applicable, our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Government payors and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and the amount of reimbursement. Coverage decisions may depend upon clinical and economic standards that disfavor new drug or biologic products when more established or lower-cost therapeutic alternatives are already available or subsequently become available. Based upon a number of factors, including clinical and economic standards, our products may not qualify for coverage and reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective;
- neither experimental nor investigational;
- prescribed by a practitioner acting within the scope of license and health plan participation agreements;
- documented adequately in the patient’s medical record;
- dispensed by a participating pharmacy; and/or
- logged and documented appropriately by the dispensing pharmacy.

The market for our products will depend significantly on access to third-party payors’ drug formularies for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. If coverage and reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In the United States, our products may be subject to discounts from list price and rebate obligations. Third-party payors have from time to time refused to include our products in their formularies, limit the type of patients for whom coverage will be provided, or restrict patient access to our products through formulary control or otherwise, in favor of less-costly generic versions of ribavirin or other treatment alternatives. Any change in formulary coverage, treatment paradigm, reimbursement levels, discounts or rebates offered on our products may impact our anticipated revenues.

In the United States, governmental and commercial third-party payors are developing increasingly sophisticated methods of controlling healthcare costs. We believe that pricing pressure for our products will continue, and future coverage and reimbursement will likely be subject to increased restrictions. For example, the PPACA, which has already imposed significant healthcare cost containment measures, also encourages the

development of comparative effectiveness research and any adverse findings for our products from such research may reduce the extent of coverage and reimbursement for our products. The PPACA created the Patient-Centered Outcomes Research Institute to review the effectiveness of treatments and medications in federally-funded healthcare programs. The PCORI publishes the results of its studies. An adverse finding result may result in a treatment or product being removed from Medicare or Medicare coverage.

Managed care organizations continue to seek price discounts and in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs, which may result in managed care organizations influencing prescription decisions for a larger segment of the population, which could constrain pricing, formulary position or reimbursement for our products. Economic pressure on state budgets may also have a similar impact on Medicaid coverage and reimbursement.

In certain countries in the European Union and some other international markets, governments provide healthcare at low-cost to consumers and regulate pharmaceutical pricing, patient eligibility or reimbursement levels to control costs for the government-sponsored healthcare system. We expect to see strong efforts to reduce healthcare costs in our international markets, including: patient access restrictions; suspensions on price increases; prospective and possibly retroactive price reductions, mandatory discounts and rebates, and other recoupments; recoveries of past price increases; and greater importation of drugs from lower-cost countries to higher-cost countries. In addition, certain countries set prices by reference to the prices in other countries where our products are marketed. Thus, our inability to secure adequate prices in a particular country may not only limit the marketing of our products within that country, but may also adversely affect our ability to obtain acceptable prices in other markets.

Healthcare reform measures could hinder or prevent our product candidates' commercial success, if approved, and could increase our costs.

In both the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is a significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding individual access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in 2010, the PPACA was enacted, which was intended to expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals, strengthening of program integrity measures and enforcement authority, and expansion of the Medicaid program. The PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Several provisions of the new law, which have varying effective dates, may affect us and will likely increase certain of our costs. In this regard, the PPACA includes the following provisions:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs that began in 2011;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- an extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- changes to the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- a new requirement to annually report drug samples that manufacturers and distributors provide to licensed practitioners or to pharmacies of hospitals or other healthcare entities;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- creation of the Independent Payment Advisory Board which has the authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs.

The reforms imposed by the new law will significantly impact the pharmaceutical industry; however, the full effects of the PPACA cannot be known until these provisions are implemented and the CMS and other federal and state agencies issue and finalize all applicable regulations or guidance. We will continue to evaluate the PPACA, the implementation of regulations or guidance related to various provisions of the PPACA by federal agencies, as well as trends and changes that may be encouraged by the legislation and that may potentially have an impact on our business over time. The cost of implementing more detailed record keeping systems and otherwise complying with these regulations could substantially increase our costs. The changes to the way our products are reimbursed by the CMS could reduce our revenues. Both of these situations could adversely affect our results of operations.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products.

International operations are also generally subject to extensive price and market regulations and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or reduce the value of our intellectual property portfolio or may make it economically unsound to launch our products in certain countries. We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. Future price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

Additionally, in some countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various European Union member states and parallel distribution or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our product candidates to other available therapies, which is time-consuming and costly. If reimbursement of our product candidates is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability of our products in such country.

If our processes and systems are not compliant with regulatory requirements, we could be subject to restrictions on marketing our products or could be delayed in submitting regulatory filings seeking approvals for our product candidates.

We have a number of regulated processes and systems that are required to obtain and maintain regulatory approval for our drugs and product candidates. These processes and systems are subject to continual review and periodic inspection by the FDA and other regulatory bodies. If compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our product candidates, or delays in obtaining regulatory approval after filing. Any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs from the market, the imposition of civil or criminal penalties or a refusal by the FDA and/or other regulatory bodies to

approve pending applications for marketing approval of new drugs or supplements to approved applications, any of which could have a material adverse effect on our business. Given the number of high profile adverse safety events associated with certain drug products, regulatory authorities may require, as a condition of approval, costly risk evaluation and mitigation strategies, which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, expedited reporting of certain adverse events, pre-approval of promotional materials and restrictions on direct-to-consumer advertising. For example, any labeling approved for any of our product candidates may include a restriction on the term of its use, or it may not include one or more intended indications. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs during the period of product development, clinical trials and regulatory review and approval, as well as increased costs to assure compliance with any new post-approval regulatory requirements. Any of these restrictions or requirements could force us or our collaborators to conduct costly studies.

In addition, we are a party to agreements that transfer responsibility for complying with specified regulatory requirements, such as packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information on the product or compliance with manufacturing requirements, to our collaborators and third-party manufacturers. Approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices ("cGMP"). As such, we and our contract manufacturers, which we are responsible for overseeing and monitoring for compliance, are subject to continual review and periodic inspections to assess compliance with cGMP. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. The FDA may hold us responsible for any deficiencies or noncompliance of our contract manufacturers in relation to our product candidates and commercial products. If our collaborators or third-party manufacturers do not fulfill these regulatory obligations, any drugs we market or for which we or they obtain approval may be deemed adulterated, which carries significant legal implications, and may be subject to later restrictions on manufacturing or sale, which could have a material adverse effect on our business.

Risks Related to Our Intellectual Property Rights

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

Our commercial success will depend, in part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our products and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our products and product candidates that are important to our business. We cannot be certain that patents will be issued or granted with respect to applications that are currently pending or that we apply for in the future with respect to one or more of our products and product candidates, or that issued or granted patents will not later be found to be invalid and/or unenforceable.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, collaboration partners, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We may license patent rights that are valuable to our business from third parties, in which event we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued, and even if issued, the patents may not meaningfully protect our products or product candidates, effectively prevent competitors and third parties from commercializing competitive products or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner. Changes in the patent laws, implementing regulations or interpretation of the patent laws in the United States and other countries may also diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. For those countries where we do not have granted patents, we may not have any ability to prevent the unauthorized use or sale of our proprietary medicines and technology or to prevent third parties from selling or importing products made using our inventions in and into the United States and other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our intellectual property rights may not be effective or sufficient to prevent them from competing.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag 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 owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. Beginning in March 2013, the United States transitioned to a first-inventor-to-file system in which, assuming the other requirements for patentability are met, the first-inventor-to-file a patent application will be entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office (U.S. PTO) or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. Participation in these proceedings can be very complex, expensive and may divert our management's attention from our core business. Furthermore, an adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

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

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

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in court.

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

Third-party claims of intellectual property infringement, misappropriation or other violation may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and *inter partes* reexamination proceedings before the U.S. PTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization and may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. Even if we or our future strategic collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property and it could require us to make substantial licensing and royalty payments.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to

pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Most of our competitors are larger than we are and have substantially greater resources and may be able to sustain the costs of complex patent litigation longer than we could. The uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or enter into strategic collaborations that would help us bring our product candidates to market.

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. For example:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or collaboration partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or collaboration partners might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages 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;
- we may not develop additional proprietary technologies that are patentable; and/or
- the patents of others may have an adverse effect on our business.

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

Risks Related to Our Dependence on Third Parties

We expect to continue to contract with third-party suppliers for the production of our commercial product portfolio as well as our developmental product candidates for clinical trial use and, if approved, for commercialization.

We currently employ third parties for the manufacturing of our commercial products and product candidates. This increases the risk that we will not have sufficient quantities of our products or product candidates within the timeframe and at an acceptable cost which could delay, prevent or impair our development or commercialization efforts. Additionally, we may not be able to quickly respond to changes in customer demand which could harm our business as a result of the inability to supply the market or an excess of inventory that we are unable to sell.

The facilities used by our contract manufacturers to manufacture our product candidates must adhere to FDA requirements, and are subject to inspections that may be conducted after we submit our marketing applications to the FDA in connection with review of our application, and on an ongoing basis relevant to postmarketing compliance. Although we are subject to regulatory responsibility for the quality of products manufactured by our contract manufacturers and oversight of their activities, we do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products. If our contract

manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will be subject to enforcement action, and if substantial noncompliance is identified and not corrected, they may be precluded from manufacturing product for the United States or other markets. In addition, although the FDA will hold us responsible for due diligence in the selection of, and oversight in the operations of, our contract manufacturers, we do not have direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority identified significant compliance concerns with our contract manufacturers, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products or product candidates, if approved.

We have agreements with third-party manufacturers for the provision of active pharmaceutical ingredient (API), drug product manufacturing and packaging of our commercial products. Reliance on third-party manufacturers carries additional risks, such as not being able to comply with cGMP or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Due to FDA requirements and other factors, we are generally unable to make changes to our supplier arrangements without delay. Manufacturing services related to each of our pharmaceutical products are primarily provided by a single source. Each of our raw materials are also provided by a single source. We attempt to mitigate this risk through long-term contracts and inventory safety stock. In the event that any of these third-party manufacturers fail regulatory compliance, fail to meet quality assurance specifications or experience an unavoidable extraordinary event, our business could be adversely affected.

Any products that we may develop may compete with other product candidates and commercialized products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure or refusal to supply on the part of our existing or future suppliers could delay clinical development, marketing approval or commercialization of our products. If our current suppliers cannot perform as agreed, we may be required to replace one or more of these suppliers. Although we believe that there are a number of potential long-term replacements to each supplier, we may incur added costs and delays in identifying and qualifying any such replacements.

We rely on third parties to store and distribute supplies for our clinical trials and for the manufacture of our product candidates. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval or our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. We are party to intellectual property license agreements with third parties and expect to enter into additional license agreements in the future. Our current license agreements impose, and we expect that future license agreements will impose, various diligence, development, commercialization, payment and other obligations. If we fail to comply with our obligations under these agreements, the licensor may have the right to terminate the license agreement or may exercise a right to have the intellectual property that we license returned. For example, under our exclusive sub-license agreement for belumosudil with NT Life Sciences, LLC and Surface Logix, Inc., if we fail to comply with our diligence obligations, the former owners of the intellectual property licensed under such agreement may require us and our licensors to return such intellectual property, in which case our license to such intellectual property would terminate. Any termination of these licenses could result in the loss of significant rights and could have a material adverse effect on our ability to commercialize our product candidates, including belumosudil.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;

- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates; and/or
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our collaboration partners.

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 are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates.

The risks that we face in connection with our current and any future collaborations include the following:

- Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our product candidates. The ability of some of our products and product candidates to reach their potential could be limited if collaborators decrease or fail to increase development or commercialization efforts related to those products or product candidates.
- Any future collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.
- Collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or product candidates that are the subject of their collaborations with us.

Our collaboration agreements are subject to termination under various circumstances.

Risks Related to Our Operations

Our business has been, and will likely continue to be adversely affected by the effects of health epidemics and pandemics, including the COVID-19 pandemic, in regions where we or third parties on which we rely have significant concentrations of clinical trial sites or other business operations. The COVID-19 pandemic has impacted our operations, including at our corporate headquarters in New York, commercial operations in Pennsylvania, clinical operations in Massachusetts, research facility in New Jersey and at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business. If these impacts continue for an extended period of time, our business could be materially and adversely affected.

Our business has been be adversely affected by health epidemics in regions where we have clinical trial sites or other business operations and could cause significant disruption in the operations of CROs upon whom we rely. For example, in response to the COVID-19 pandemic we implemented work-from-home policies and other measures directed at employee safety. These policies have impacted productivity in certain business units, impacted management attention, depleted resources, disrupted our business and delayed our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar disruptions in our operations could materially and adversely impact our business, operating results and financial condition. In addition, our clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. For instance, due to interruptions at clinical sites, enrollment has been delayed in our ongoing Phase 2 clinical trial of belumosudil (KD025) in systemic sclerosis and enrollment was also delayed in our ongoing Phase 1 clinical trial of KD033 in patients with metastatic or locally advanced solid tumors. Also, some patients may not be able to comply with clinical trial protocols if quarantine impedes patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations. The COVID-19 pandemic may materially affect us economically. While the economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, the widespread pandemic has resulted in significant disruption of global financial markets, potentially reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

Our business could be adversely affected by the cyber, privacy and productivity effects of remote working and disruption at management and board levels due to COVID-19.

We have transitioned all of our employee population to a remote work environment in an effort to mitigate the spread of COVID-19, which may exacerbate certain risks to our business, including an increased demand for information technology resources, increased risk of phishing and other cybersecurity attacks, and increased risk of unauthorized dissemination of sensitive personal information or proprietary or confidential information about us or our members or other third-parties. We may experience disruptions to our business operations resulting from quarantines, self-isolations, or other movement and restrictions on the ability of our employees to perform their jobs that may impact our ability to progress our clinical candidates in a timely manner or meet development milestones. The COVID-19 pandemic could also disrupt our operations due to absenteeism by infected or ill members of management or other employees, or absenteeism by members of management and other employees who elect not to come to work due to the illness affecting others in our office or laboratory facilities, or due to quarantines. COVID-19 illness could also impact members of our Board of Directors resulting in absenteeism from meetings of the directors or committees of directors, and making it more difficult to convene the quorums of the full Board of Directors or its committees needed to conduct meetings for the management of our affairs.

We may not be entitled to forgiveness of our recently received loan under the Paycheck Protection Program of the Coronavirus Aid, Relief, and Economic Security Act, and our application for the Paycheck Protection Program Loan could in the future be determined to have been impermissible or could damage our reputation.

On April 14, 2020 we received proceeds of $3.1 million from a loan under the Paycheck Protection Program (“PPP Loan”) of the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”), which we intend to use to retain current employees, maintain payroll and make lease and utility payments. The PPP Loan matures on April 15, 2022 and bears interest at a rate of 1% per annum. On August 20, 2020, the loan was amended so that, commencing August 15, 2021, we are required to pay the lender equal monthly payments of principal and interest as required to fully amortize by April 15, 2022 the principal amount outstanding on the PPP Loan as of

October 15, 2020. Under the CARES Act, loan forgiveness is available for the sum of documented payroll costs, covered rent payments, covered mortgage interest and covered utilities during the eight-week period beginning on the date of loan approval. We will be required to repay any portion of the outstanding principal that is not forgiven, along with accrued interest. While we have begun preparations to apply for forgiveness, we cannot provide any assurance that we will be eligible for loan forgiveness, or that any amount of the PPP Loan will ultimately be forgiven by the U.S. Small Business Administration ("SBA"). Furthermore, on April 28, 2020, the Secretary of the U.S. Department of the Treasury stated that the SBA will perform a full review of any PPP loan over $2.0 million before forgiving the loan.

In order to apply for the PPP Loan, we were required to certify, among other things, that the current economic uncertainty made the PPP Loan request necessary to support our ongoing operations. We made this certification in good faith after analyzing, among other things, the maintenance of our entire workforce, notwithstanding certain obvious "work-from-home" limitations associated with the nature of our business and managing risks to our development programs. In considering our position, we, an emerging growth clinical-stage biopharmaceutical research and development company with approximately 120 employees at the time of application (including 27 research staff ordinarily located within our laboratories), currently conducting 6 clinical trials to develop at least 3 medicines for currently unmet and under-served medical needs, took into account our classification as a smaller reporting company under SEC rules, our ability to currently access alternative forms of capital in the current market environment, and that management expressed substantial doubt as described in Note 1 of the financial statements in our Annual Report on Form 10-K filed with the SEC on March 5, 2020 about our ability to continue as a going concern based upon our recurring and continuing losses from operations and our need for additional funding to continue operations. The report of our independent registered public accounting firm BDO USA, LLP also included an explanatory paragraph expressing substantial doubt about our ability to continue as a going concern. Following this analysis, we believe that we satisfied all eligibility criteria for the PPP Loan, and that our receipt of the PPP Loan is consistent with the broad objectives of the PPP of the CARES Act, and following receipt of the loan, we have made no COVID-19 layoffs. The certification described above did not contain any objective criteria and is subject to interpretation. We will continue to assess our continued qualification if and when updated guidance is released by the Treasury Department. If, despite our good-faith belief that given our circumstances we satisfied all eligible requirements for the PPP Loan, we are later determined to have violated any applicable laws or regulations or it is otherwise determined that we were ineligible to receive the PPP Loan, we may be required to repay the PPP Loan in its entirety and/or be subject to additional penalties, which could also result in adverse publicity and damage to reputation. In addition, our receipt of the PPP Loan may result in adverse publicity and damage to our reputation, and a review or audit by the SBA or other government entity or claims under the False Claims Act could consume significant financial and management resources. If these events were to transpire, they could have a material adverse effect on our business, results of operations and financial condition.

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

The biopharmaceutical industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities. This may limit their availability to us.

In order to induce valuable employees to continue their employment with us, we have provided equity incentives that vest over time. The value to employees of equity incentives that vest over time is significantly affected by the success of our operations and clinical trials for our product candidates, much of which is beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Our employment arrangements generally provide for

at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses and institutions. Many of the other companies and institutions that we compete with for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

If we are unable to successfully implement our strategic plan, our business may be materially harmed.

We plan to continue to develop and commercialize novel drugs for significant unmet medical needs while we continue to market our commercial products to eligible patients to generate revenue. Absent a successful launch of one or more of our product candidates, we expect our total revenue to decline significantly. In order to maintain a strong financial position, we are focusing our investment on development programs for our most advanced product candidates. In an effort to mitigate our drug development risk and improve our chance of ultimate commercial success, we are developing multiple product candidates in a variety of disease indications. There can be no assurance that our development programs will be successful or that our research programs will result in drugs that we can successfully develop and commercialize.

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our equity holders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management’s attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and/or
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

If we acquire or license technologies, products or product candidates, we will incur a variety of costs and may never realize benefits from the transaction.

If appropriate opportunities become available, we might license or acquire technologies, resources, drugs or product candidates. We might never realize the anticipated benefits of such a transaction, and we may later incur impairment charges related to assets acquired in any such transaction. In particular, due to the risks inherent in drug

development, we may not successfully develop or obtain marketing approval for the product candidates we acquire. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

At December 31, 2020, we had 127 full-time employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, sales, marketing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of their attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations which may result in weaknesses in our infrastructure, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively with others in our industry will depend, in part, on our ability to effectively manage any future growth.

A disruption in our computer networks, including those related to cybersecurity, could adversely affect our financial performance.

We rely on sophisticated information technology systems to operate our business. These systems are potentially vulnerable to malicious intrusion, random attack, loss of data privacy, or breakdown. Although we have invested in the protection of our data and information technology and also monitor our systems on an ongoing basis, there can be no assurance that these efforts will prevent breakdowns or breaches in our information technology systems that could adversely affect our business.

We rely on our computer networks and systems, some of which are managed by third parties, to manage and store electronic information (including sensitive data such as confidential business information and personally identifiable data relating to employees, customers and other business partners), and to manage or support a variety of critical business processes and activities. We may face threats to our networks from unauthorized access, security breaches and other system disruptions. Despite our security measures, our infrastructure may be vulnerable to external or internal attacks. Any such security breach may compromise information stored on our networks and may result in significant data losses or theft of sensitive or proprietary information. In addition, a cybersecurity attack could result in other negative consequences, including disruption of our internal operations, increased cybersecurity protection costs, lost revenue, regulatory actions or litigation. Any disruption could also have a material adverse impact on our operations. We have not experienced any known attacks on our information technology systems that have resulted in any material system failure, accident or security breach to date.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

Our net operating loss (“NOL”) carryforwards could expire unused and be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under U.S. tax law. NOLs generated in taxable years beginning before January 1, 2018 are permitted to be carried forward for only 20 taxable years under applicable U.S. federal income tax law. Under the Tax Cuts and Jobs Act, or the Tax Act, as modified by the CARES Act, NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such NOLs generally will be limited in taxable years beginning after December 31, 2020 to 80% of current year taxable income. The extent to which state income tax law will conform to the Tax Act and CARES Act is uncertain. As of December 31, 2019, we had net operating loss (“NOL”) carryforwards for U.S. federal and state income tax purposes of approximately $371.1 million and $307.2 million, respectively. These carryforwards expire at various dates through December 31, 2037, with the exception of approximately $79.9 million of U.S. federal NOL carryforwards, which will not expire.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” (as defined under Section 382 of the Code and applicable

Treasury Regulations) is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. We have undergone ownership changes in the past and, accordingly, our NOLs are subject to limitation. It is possible that we have in the past undergone and may in the future undergo, additional ownership changes that we have not identified, including in connection with conversion of the notes, which could result in additional limitations on our NOLs. Furthermore, our ability to utilize NOLs of companies that we acquire may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes. For these reasons, we may not be able to utilize a material portion of the NOLs reflected on our balance sheet, even if we attain profitability, which could result in increased future tax liabilities to us and could adversely affect our operating results and financial condition.

Risks Related to Our Common Stock

We expect that our stock price will fluctuate significantly.

The trading prices of the securities of pharmaceutical and biotechnology companies have been highly volatile. The trading price of our common stock also may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section, these factors include:

- adverse results or delays in the planned clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our products and product candidates, including clinical trial requirements for approvals;
- our inability to obtain or delays in obtaining adequate product supply for any approved product or inability to do so at acceptable prices;
- failure to commercialize our product candidates or if the size and growth of the markets we intend to target fail to meet expectations;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introductions or announcements of new products offered by us or significant acquisitions, strategic collaborations, joint ventures or capital commitments by us, our collaborators or our competitors and the timing of such introductions or announcements;
- our ability or inability to effectively manage our growth;
- changes in the structure of healthcare payment systems;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- market conditions in the pharmaceutical and biotechnology sectors or the economy generally;
- our ability or inability to raise additional capital through the issuance of equity or debt or collaboration arrangements and the terms on which we raise it;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; and/or
- significant lawsuits, including patent or stockholder litigation.

The stock market in general, and market prices for the securities of biopharmaceutical companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the

market price of our common stock, regardless of our operating performance. Stock prices of many pharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. In several recent situations when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

Future sales of our common stock or securities convertible into our common stock in the public market could cause our stock price to fall.

Our stock price could decline as a result of sales of a large number of shares of our common stock or securities convertible into our common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Certain holders of our shares have rights requiring us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, subject to certain conditions. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market stand-off and lock-up agreements, Rule 144 and Rule 701 under the Securities Act, as well as, to the extent applicable, under the registration statement on Form S-8 that we have filed.

Once we register the offer and sale of shares for the holders of registration rights and shares to be issued under our equity incentive plans, they can be freely sold in the public market upon issuance or resale (as applicable).

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. In addition, any future testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. However, for as long as we are an “emerging growth company” under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an emerging growth company for up to five years following the date of our IPO. An independent assessment of the effectiveness of our internal controls could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

Holders of our convertible preferred stock may exert substantial influence over us and may exercise their control in a manner adverse to your interests.

So long as shares of our convertible preferred stock remain outstanding, without the consent of at least a majority of the then outstanding shares of the convertible preferred stock, we may not (i) authorize or approve the issuance of any convertible preferred stock, senior securities or parity securities (or, in each case, any security convertible into, or convertible or exchangeable therefor or linked thereto) or authorize or create or increase the

authorized amount of any convertible preferred stock, senior securities or parity securities (or, in each case, any security convertible into, or convertible or exchangeable therefor or linked thereto); (ii) authorize or approve the purchase or redemption of any parity securities or junior securities; (iii) amend, alter or repeal any of the provisions of the certificate of designations, our certificate of incorporation or our by-laws in a manner that would adversely affect the powers, designations, preferences and rights of the convertible preferred stock; (iv) contract, create, incur, assume or suffer to exist any indebtedness or guarantee any such indebtedness with an aggregate value of more than $5,000,000 (subject to certain exceptions); or (v) agree to take any of the above actions. The holders of convertible preferred stock will have one vote for each share of common stock into which such holders' shares could then be converted at the time, and with respect to such vote, will have voting rights and powers equal to the voting rights and powers of the holders of our common stock.

The certificate of designations governing the convertible preferred stock also provides that no amendment or waiver of any provision of the certificate of designations or our charter or bylaws shall, without the prior written consent of all holders of the convertible preferred stock who are known to us to hold, together with their affiliates, more than 5% of the convertible preferred stock then outstanding (i) reduce any amounts payable or that may become payable to holders of the convertible preferred stock; (ii) postpone the payment date of any amount payable to holders of the convertible preferred stock or waive or excuse any payment; (iii) modify or waive the conversion rights of the convertible preferred stock in a manner that would adversely affect any holder of the convertible preferred stock; or (iv) change any of the voting-related provisions or any other provision of the certificate of designations specifying the number or percentage of holders of the convertible preferred stock which are required to waive, amend or modify any rights under the certificate of designations or make any determination or grant any consent under that document.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, our certificate of incorporation and bylaws:

- permit the board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly-created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum; and
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be taken by written consent.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any stockholder owning in excess of 15.0% of our outstanding stock for a period of three years following the date on which the stockholder obtained such 15.0% equity interest in us.

Our management has broad discretion in using cash, cash equivalents and marketable debt securities and our other capital resources.

We expect to continue to use our cash, cash equivalents and marketable debt securities and our other capital resources to fund the clinical development of our pipeline and for general corporate purposes. Our management has broad discretion in the application of our cash, cash equivalents and marketable debt securities and our other capital resources and could spend the funds in ways that do not improve our results of operations or enhance the value of our equity. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, diminish available cash flows available to service our debt, cause the value of our equity to decline and delay the development of our product candidates. Pending their use, we may

invest cash, cash equivalents and marketable debt securities and our other capital resources in a manner that does not produce income or that loses value.

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

We have never declared or 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. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our equity securities will likely be your sole source of gain for the foreseeable future.

Future sales and issuances of equity securities, convertible securities or other securities could result in additional dilution of the percentage ownership of holders of our common stock.

We expect that additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell equity securities, convertible securities or other securities in one or more transactions at prices and in a manner we determine from time to time. If we sell equity securities, convertible securities or other securities in more than one transaction, investors in such future offerings may be materially diluted by subsequent sales. Such sales would also likely result in material dilution to our existing equity holders, and new investors could gain rights, preferences and privileges senior to those of holders of our existing equity securities.