Filed pursuant to Rule 424(b)(4)
Registration No. 333-242334

PROSPECTUS

6,062,500 Shares of Common Stock

This prospectus relates to the offer and sale from time to time by the selling stockholders identified in the section entitled "Selling Stockholders" of up to an aggregate of 6,062,500 shares of our common stock.

The shares of common stock described in this prospectus or in any supplement to this prospectus may be sold from time to time pursuant to this prospectus by the selling stockholders in ordinary brokerage transactions, in transactions in which brokers solicit purchases, in negotiated transactions, or in a combination of such methods of sale, at market prices prevailing at the time of sale, at prices related to such prevailing market prices, at fixed prices or prices subject to change, or at negotiated prices. See "Selling Stockholders" and "Plan of Distribution." We cannot predict when or in what amounts the selling stockholders may sell any of the shares offered by this prospectus.

We are not selling any shares of our common stock, and we will not receive any of the proceeds from the sale of shares by the selling stockholders. The selling stockholders will pay all brokerage fees and commissions and similar sale-related expenses. We are only paying expenses relating to the registration of the shares with the U.S. Securities and Exchange Commission. The registration of the shares of our common stock does not necessarily mean that any of such shares will be offered or sold by the selling stockholders.

A supplement to this prospectus may add, update or change information contained in this prospectus. You should read this prospectus and any prospectus supplement, together with the documents we incorporate by reference, carefully before you invest.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CYCN." On August 6, 2020, the last reported sale price of our common stock on the Nasdaq Global Select Market was $4.16.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" BEGINNING ON PAGE 7 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT OR ANY DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS BEFORE INVESTING IN OUR SECURITIES.

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

The date of this prospectus is August 17, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the "SEC"), using a "shelf" registration process for the delayed offering and sale of securities pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"). Under this shelf registration process, the selling stockholders named in this prospectus or any supplement to this prospectus may, over time, offer and sell the securities described in this prospectus. This prospectus provides you with a general description of our common stock. The selling stockholders are required to provide you with this prospectus and, in certain cases, a prospectus supplement containing specific information about the selling stockholders and the terms upon which the securities are being offered. A prospectus supplement may also add, update or change information contained in this prospectus. Each time we offer securities under this prospectus, we will provide a prospectus supplement or other offering materials that will contain specific information about the terms of that offering. You should read both this prospectus and any prospectus supplement together with the additional information described under the headings "*Information Incorporated by Reference*" and "*Where You Can Find More Information*" below.

We may also add, update or change information contained in this prospectus by means of a prospectus supplement or by incorporating by reference information that we file or furnish to the SEC. The registration statement that we filed with the SEC includes exhibits that provide more detail on the matters discussed in this prospectus. If the information in this prospectus is inconsistent with a prospectus supplement, you should rely on the information in that prospectus supplement. Please carefully read this prospectus and any prospectus supplement, together with the additional information described under the headings "*Information Incorporated by Reference*" and "*Where You Can Find More Information*" before purchasing any securities.

You should rely only on the information contained or incorporated by reference in this prospectus, any prospectus supplement and any issuer free writing prospectus. "Incorporated by reference" means that we can disclose important information to you by referring you to another document filed separately with the SEC. We have not authorized any other person to provide you with different information. If anyone provides you with different information, you should not rely on it. We are not making an offer of these securities in any state or jurisdiction where the offer is not permitted. You should only assume that the information in this prospectus or in any prospectus supplement or issuer free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context requires otherwise, references in this prospectus to "Cyclerion," the "Company," the "registrant," "we," "us," and "our" refer to Cyclerion Therapeutics, Inc. and, where appropriate, our consolidated subsidiaries, and references in this prospectus to "Ironwood" refer to Ironwood Pharmaceutics, Inc. and, where appropriate, its consolidated subsidiaries.

CAUTIONARY NOTE CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, including the documents incorporated by reference into this prospectus and any accompanying prospectus supplement, contain 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 (the "Exchange Act"). Such forward-looking statements involve substantial risks and uncertainties. All statements in this prospectus, other than statements of historical facts, including statements about future events, financing plans, financial position, business strategy, budgets, projected costs, plans and objectives of management for future operations, are forward-looking statements that involve certain risks and uncertainties. Use of the words "may," "might," "will," "would," "could," "should," "believes," "estimates," "projects," "potential," "expects," "plans," "seeks," "intends," "evaluates," "pursues," "anticipates," "continues," "designs," "impacts," "affects," "forecasts," "target," "outlook," "initiative," "objective," "designed," "priorities," "goal" or the negative of those words or other similar expressions may identify forward-looking statements that represent our current judgment about possible future events, but the absence of these words does not necessarily mean that a statement is not forward-looking.

Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. Because forward-looking statements relate to the future, by their nature, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. As a result, our actual results may differ materially from those contemplated by the forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include regional, national or global political, economic, business, competitive, market and regulatory conditions and the following:

- the COVID-19 pandemic affecting our activities in ways that are difficult to precisely judge at this time;
- our relationships with third parties, collaborators and our employees;
- our ability to execute our strategic priorities;
- our ability to finance our operations and business initiatives and obtain funding for such activities;
- the timing, investment and associated activities involved in developing, obtaining regulatory approval for, launching and commercializing our product candidates, including olinciguat and IW-6463;
- our interpretation of the data from the praliciguat Phase 2 clinical trial in patients with diabetic nephropathy, including regarding the clinical site whose results appear to be inconsistent with the overall study population;
- the potential of further evaluation of praliciguat;
- the potential commercial opportunities of praliciguat, including the potential value of an out-license of praliciguat by us;
- our ability to identify a licensee and to negotiate and execute an out-license or similar agreement with respect to praliciguat;
- the impact on our business of our recent workforce and expense reduction initiatives;
- our plans with respect to the development, manufacture or sale of our product candidates and the associated timing thereof, including the design and results of pre-clinical and clinical studies;
- the safety profile and related adverse events of our product candidates;
- the efficacy and perceived therapeutic benefits of our product candidates, their potential indications and their market potential;
- U.S. and non-U.S. regulatory requirements for our product candidates, including any post-approval development and regulatory requirements, and the ability of our product candidates to meet such requirements;

- our ability to attract and retain employees needed to execute our business plans and strategies and our ability to manage the impact of any loss of key employees;
- our ability to obtain and maintain intellectual property protection for our product candidates and the strength thereof;
- our future financial performance, revenues, expense levels, payments, cash flows, profitability, tax obligations, capital raising and liquidity sources, real estate needs and concentration of voting control, as well as the timing and drivers thereof, and internal control over financial reporting;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with our product candidates;
- the impact of government regulation in the life sciences industry, particularly with respect to healthcare reform;
- potential indemnification liabilities we may owe to Ironwood after the Separation;
- the tax treatment of the distribution and the limitations imposed on us under the tax matters agreement that we entered into with Ironwood; and
- trends and challenges in the markets for our potential products.

The preceding list is not intended to be an exhaustive list of all forward-looking statements in this prospectus and any accompanying prospectus supplement. You should read this prospectus and any accompanying prospectus supplement with the understanding that actual future results, levels of activity, performance and achievements may be materially different from what is currently expected. We qualify all of the forward-looking statements by these cautionary statements. Additional factors that could cause results to differ materially from those described above can be found in the reports and information that we file with the SEC from time to time.

SUMMARY INFORMATION

This summary does not contain all the information that you should consider before investing in our Company. You should carefully read the entire prospectus and any accompanying prospectus supplement, including all documents incorporated by reference herein and therein.

Company Overview

We are a clinical-stage biopharmaceutical company focused on soluble guanylate cyclase, or sGC, pharmacology to discover, develop and commercialize treatments for serious and orphan diseases. We seek to enable the full therapeutic potential of next-generation sGC stimulators. sGC stimulators are small molecules that act synergistically with nitric oxide on sGC to boost production of cyclic guanosine monophosphate, or cGMP. cGMP is a key second messenger that, when produced by sGC, regulates diverse and critical biological functions throughout the body including blood flow and vascular dynamics, inflammatory and fibrotic processes, metabolism and neuronal function. We believe that the key to unlocking the full therapeutic potential of the nitric oxide-cGMP pathway is to design differentiated next-generation sGC stimulators that preferentially modulate pathway signaling in tissues of greatest relevance to the diseases they are developed to treat back to the appropriate physiological range of activity. We are led by an accomplished team, with a track record of discovering, developing and commercializing meaningful therapies for patients while creating value for stockholders and with a long history of experience in the NO-sGC-cGMP pathway.

The core of our research and development strategy is to harness the power of sGC pharmacology to develop therapies for serious and orphan diseases. Our portfolio of programs includes:

- *Olinciguat.* Sickle cell disease (SCD) is a genetic disorder affecting approximately 100,000 people in the United States and approximately 50,000 in the EU5, or France, Germany, Italy, Spain and the United Kingdom. By amplifying nitric oxide signaling, we believe that olinciguat has the potential to reduce the proportion of sickled cells, as well as improve blood flow, endothelial integrity, and vascular inflammation. For patients with SCD, we believe this may translate into reduction in debilitating daily symptoms such as chronic pain and fatigue, decrease in anemia, reduction in painful VOCs and end-organ protection (e.g. kidney and lung) potentially leading to an increase in survival. Olinciguat is an orally administered, once-daily, vascular sGC stimulator that we believe is well suited for the treatment of SCD given its distribution to the vasculature and highly perfused organs, such as the kidney and lungs, which are frequently affected by the disease. Olinciguat has been granted Orphan Drug Designation for SCD by the U.S. Food and Drug Administration (the "FDA") and is currently conducting closeout activities in a Phase 2 study, STRONG-SCD. We expect topline data from this study in late Q3 2020.
- *Praliciguat.* Praliciguat is an orally administered, once-daily systemic sGC stimulator that we believe is well suited for the treatment of serious cardiometabolic diseases given its extensive distribution into tissues, particularly adipose, kidney, heart and liver. Praliciguat was evaluated in two Phase 2 proof-of-concept studies: a dose-ranging study in 156 adult patients with diabetic nephropathy, and a study in 196 adult patients with heart failure with preserved ejection fraction (HfpEF), CAPACITY-HfpEF. On October 30, 2019, we released topline results from these studies.
    - The study of praliciguat in participants with DN did not meet statistical significance on its primary endpoint of reduction in albuminuria from baseline as compared to placebo, measured by urine albumin creatinine ratio (UACR), but there was a trend toward improvement across the total intention-to-treat (ITT) study population. During statistical validation, data from one clinical trial site were found to be inconsistent with those of the overall study population. At this site, a greater percentage of participants assigned to the praliciguat treatment arms had undetectable or very low praliciguat plasma concentrations and larger reductions in albuminuria than was seen across the broader study population. In a post-hoc sensitivity analysis in which data from this site were excluded, an increased treatment effect and reduced variability were observed. In addition, trends towards improvements were observed in participants treated with praliciguat in several secondary vascular and metabolic measures associated with cardiovascular

risk and kidney disease progression, including blood pressure, cholesterol and HbA1c levels, compared to placebo. Praliciguat was generally well tolerated, and the safety profile supports further clinical investigation.

- The study in HFpEF did not meet statistical significance on its primary endpoint of improved exercise capacity from baseline as compared to placebo, measured by cardiopulmonary exercise testing (CPET). There was clear evidence of drug exposure and pharmacological activity as judged by expected reductions in blood pressure. Praliciguat was generally well tolerated, and the safety profile supports investigation of praliciguat in other indications. A positive trend in reducing HbA1c levels was observed in the subset of participants with diabetes. This is consistent with the results observed in the Phase 2 study of praliciguat in diabetic nephropathy. We are discontinuing development of praliciguat in HFpEF.
- The Company is in the process of seeking an out-license of praliciguat.

- *IW-6463*. IW-6463 is an orally administered central nervous system (CNS)-penetrant sGC stimulator that, because it readily crosses the blood-brain barrier, affords an unprecedented opportunity to expand the utility of sGC pharmacology to serious CNS diseases. Nitric oxide is one of several fundamental neurotransmitters, yet it has not been leveraged for its therapeutic potential in the CNS. In preclinical studies, IW-6463 has been associated with increased cerebral blood flow, reduced markers of neuroinflammation, improved neuronal health, neuroprotective effects and enhanced cellular bioenergetics and mitochondrial function.
  - On January 13, 2020, we announced positive Phase 1 study results that provide the foundation for continued development of IW-6463. The Phase 1 healthy participant study results indicate that IW-6463 was well tolerated. Pharmacokinetic (PK) data, obtained from both blood and cerebral spinal fluid, support once-daily dosing with or without food and demonstrated IW-6463 penetration across the blood-brain-barrier at levels expected to be pharmacologically active. We believe that these results, together with preclinical data, provide strong support for continued development of IW-6463 as a potential new medicine for serious neurodegenerative diseases.
  - A translational pharmacology study in approximately 24 elderly participants is ongoing. This study will evaluate safety, PK, and measures of CNS pharmacological activity, including cerebral blood flow by MRI. Topline data from that study is expected in mid-Q3 2020.
  - The Company anticipates initiating two parallel exploratory Phase 2 studies of IW-6463 to evaluate safety and a variety of efficacy measures, including engagement of CNS biomarkers using novel trial designs in Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like Episodes (MELAS) and Alzheimer's disease with vascular features (ADv). These studies are designed to de-risk and direct future development in CNS diseases.
- *Discovery Research*. The Company has ongoing discovery research work, focused primarily on:
  - Our orally administered liver-targeted sGC stimulator is designed to selectively partition to the liver. By achieving liver concentrations many fold higher than corresponding plasma concentrations, we intend to maximize hepatic pharmacology. In animal models of liver fibrosis treated with systemic sGC stimulators, we have observed reductions in liver fibrosis, inflammation and steatosis, pathophysiological processes that underlie multiple chronic liver diseases.
  - Our lung-targeted sGC stimulator will be administered via inhalation and will be aimed at realizing the full potential of sGC stimulation in pulmonary diseases by selectively increasing exposure in the lung. By achieving significantly greater selectivity for lung over plasma, we intend to maximize pulmonary pharmacology.
  - Additional discovery efforts are ongoing and aimed at further expanding the potential of sGC stimulation in disorders of the CNS.

The Separation, Distribution and 2019 Private Placement

On April 1, 2019, Ironwood completed the separation of its sGC business, and certain other assets and liabilities, into us as a separate, independent publicly traded company by way of a pro-rata distribution of

our common stock through a dividend distribution of one share of our common stock, with no par value per share, for every 10 shares of Ironwood common stock held by Ironwood stockholders as of the close of business on March 19, 2019, the record date for the distribution (the "Separation.") As a result of the Separation, we became an independent public company and commenced trading under the symbol "CYCN" on the Nasdaq Global Select Market on April 2, 2019.

In connection with the Separation, on March 30, 2019, we entered into certain agreements with Ironwood to provide a framework for our relationship with Ironwood following the Separation, including, among others, a Separation Agreement, a Tax Matters Agreement, and an Employee Matters Agreement. In addition, in connection with the Separation, on April 1, 2019, we entered into a Development Agreement, an Ironwood Transition Services Agreement, a Cyclerion Transition Services Agreement and an Intellectual Property License Agreement with Ironwood. For certain risks associated with the Separation, see "*Risk Factors — Risks Related to the Separation*."

On April 2, 2019, we issued 11,817,165 shares of our common stock (the "Private Placement Shares"), to accredited investors for gross proceeds of $175 million (net proceeds of approximately $165 million) pursuant to the Amended and Restated Common Stock Purchase Agreement. We received the funds associated with the sale of the Private Placement Shares on April 2, 2019.

Corporate Information

We were incorporated in the Commonwealth of Massachusetts on September 6, 2018. Our principal executive offices are located at 301 Binney Street, Cambridge, MA 02142. Our telephone number is (857) 327-8778. Our common stock is listed on the Nasdaq Global Select Market under the symbol "CYCN."

Stock Purchase Agreement

On July 29, 2020, the Company entered into a Common Stock Purchase Agreement (the "Purchase Agreement") with selling stockholders for the private placement of 6,062,500 shares of the Company's common stock, at a purchase price of $4.00 per share (the "PIPE Transaction"). The closing of the PIPE Transaction occurred on July 29, 2020. The Company did not utilize the services of a placement agent or broker in connection with the PIPE Transaction and accordingly incurred no material related transaction fees or commissions. Pursuant to the Purchase Agreement, the Company is required to file a registration statement with the Securities and Exchange Commission under the Securities Act, covering the resale of the shares purchased in the PIPE Transaction and to obtain and maintain effectiveness thereof for up to three years, subject to certain exceptions and penalties.

The shares sold in the PIPE Transaction were issued and sold to "accredited investors" (as defined by Rule 501 under the Securities Act, as amended) in reliance upon exemptions from registration afforded by Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated thereunder and corresponding provisions of state securities laws.

The foregoing description of the Purchase Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the form of the Purchase Agreement filed as Exhibit 10.1 hereto.

RISK FACTORS

An investment in our securities involves risks. We urge you to carefully consider all of the information contained in or incorporated by reference in this prospectus and other information which may be incorporated by reference in this prospectus or any prospectus supplement as provided under "Information Incorporated by Reference." This prospectus also contains forward-looking statements that involve risks and uncertainties. Please read "Cautionary Note Concerning Forward-Looking Statements."

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this prospectus or in any prospectus supplement and in the documents incorporated by reference into this prospectus or any prospectus supplement. You should carefully consider the risks described below, in addition to the other information contained in this prospectus and in any prospectus supplement and in the documents incorporated by reference into this prospectus or any prospectus supplement. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations. If any of these risks occur, this could expose us to liability, and our business, financial condition or results of operation could be adversely affected. As a result, you could lose all or part of your investment.

Risks Related to Our Financial Position and Capital Needs

As we are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale, valuing our business and predicting our prospects is challenging.

We are a clinical-stage biopharmaceutical company that was incorporated in 2018. Our business was conducted within Ironwood prior to that time, and we had no history as an independent company prior to the completion of the Separation. We are developing a pipeline of sGC stimulators, but we have no products approved for commercial sale, and we have never generated revenue from product sales. Our operating activities to date have been limited primarily to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, pursuing partnership opportunities and conducting early stage clinical trials for our most advanced product candidates, praliciguat, olinciguat and IW-6463.

To date, we have not obtained marketing approval for any of our product candidates, engaged, on our own or through a third party, in commercial scale manufacturing, or conducted sales and marketing activities necessary for the successful commercialization of our product candidates. Our short operating history offers limited insight into our prospects for success or even viability. We expect our operating performance to fluctuate. We will encounter challenges frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields and we have not yet demonstrated an ability to successfully navigate such challenges. If we do not successfully address the challenges we face, our business, prospects, financial condition and results of operations will be materially harmed.

Our business has incurred significant losses and we anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated revenue from product sales and may never be profitable.

Our business has incurred operating losses due to costs incurred in connection with our research and development activities and general and administrative expenses associated with our operations. Our net losses for the years ended December 31, 2018 and 2019 were $115.3 million and $123.0 million, respectively. We expect to incur significant losses for several years, as we continue our research activities and conduct development of, and seek regulatory approvals for, our product candidates.

Our ability to generate revenue from our product candidates and achieve profitability depends on our ability, alone or with strategic partners, to complete the development of, and obtain the necessary regulatory and essential pricing and reimbursement approvals to commercialize, our product candidates. We do not know when, if ever we will generate revenues from sales of our products.

Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency (the "EMA"), or other regulatory agencies, domestic or foreign, to perform clinical and

other studies in addition to those that we currently anticipate. Even if one or more of the product candidates that we develop is approved for commercial sale, we may never generate revenue in amounts sufficient to achieve and maintain profitability.

We will need to raise additional funding to advance our product candidates, which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations. Raising additional capital may dilute our existing shareholders, restrict our operations or cause us to relinquish valuable rights.

As of December 31, 2019, we had unrestricted cash and cash equivalents of approximately $94.9 million. Our management believes that such cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements through the first quarter of 2021. However, we will require significant additional funding to advance our product candidates, alone or with strategic partners, through clinical studies and to seek marketing approval, as well as to continue advancing our research and development efforts with our other product candidates. We may also need to raise additional funds sooner than currently anticipated if we choose to pursue additional indications or geographies for our product candidates, identify additional product candidates to advance through clinical development or otherwise expand more rapidly than we presently anticipate. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. We are seeking funds through collaborations, strategic alliances, or licensing arrangements with third parties, and such agreements may impact rights to our product candidates or technologies, future revenue streams, research programs or products candidates or to grant licenses on terms that may not be favorable to us. Such arrangements will limit our participation in the success of any of our product candidates that receive regulatory approval.

We may also seek to raise such capital through public or private equity, royalty financing or debt financing. Raising funds in the then-current economic environment may be challenging, and such financing may not be available in sufficient amounts or on acceptable terms, if at all. The terms of any financing may harm existing shareholders. The issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities may dilute the ownership of existing shareholders. Incurring debt would result in increased fixed payment obligations, and we may agree to restrictive covenants, such as limitations on our ability to incur additional debt or limitations on our ability to acquire, sell or license intellectual property rights that could impede our ability to conduct our business. Regardless of the terms of our debt or equity financing, our agreements and obligations under the tax matters agreement with Ironwood limits our ability to issue stock. See "*Risk factors — Risks Related to the Separation*."

If we are unable to raise capital when needed or on reasonable terms, we may curtail, delay or discontinue our research or development programs, scale back or cease any commercialization efforts or wind down our business. In addition, such additional fundraising efforts may divert our management from their day-to-day activities, which may impede our ability to develop and commercialize our product candidates.

Risks Related to our Business and Industry

The "target-to-disease" approach we are taking to discover and develop product candidates targeting cGMP, may never lead to marketable products.

We have concentrated our product research and development efforts to date on a "target-to-disease" approach to the treatment of diseases involving the cGMP pathway and/or sGC signaling, so our future success depends on the successful development of our pipeline of sGC stimulators. The scientific evidence to support the feasibility of developing our product candidates is both preliminary and limited. If we do not successfully develop and commercialize product candidates based upon our "target-to-disease" approach, we will not become profitable and the value of our common stock may decline.

Further, our focus solely on developing a pipeline of sGC stimulators, instead of multiple, more proven technologies, increases the risks associated with the ownership of our common stock. If we are not successful in developing any product candidates using our sGC platform, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and

implement successfully an alternative product development strategy, which would materially harm our business, prospects, financial condition and results of operations.

Research and development of biopharmaceutical products is inherently risky. We may encounter substantial delays in our clinical studies, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Our current product candidates are at an early stage of development. Our business depends heavily on successful preclinical development, clinical testing, regulatory approvals and commercialization of our lead product candidates. On October 30, 2019, we announced that our topline results from our Phase 2 proof-of-concept trials of praliciguat in participants with diabetic nephropathy and in HFpEF did not meet statistical significance on their respective primary endpoints. In light of this topline data, we do not intend to continue development of praliciguat in participants with HFpEF. However, there was a trend towards improvement across the total intention-to-treat diabetic nephropathy study population and praliciguat was generally well tolerated, therefore, as previously announced, we intend to pursue an out-license of praliciguat. Our other lead product candidates, olinciguat and IW-6463, as well as any other of our current product candidates or product candidates that we may discover in the future, will require regulatory approvals resulting from substantial additional development and testing prior to commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical and clinical studies that our product candidates are both safe and effective for use in each target indication. Each product candidate must demonstrate an adequate benefit-risk profile for its intended use in its intended patient population. In some instances, significant variability in safety or efficacy appear in different clinical studies of the same product candidate due to numerous factors, including changes in study protocols, differences in the number and characteristics of the enrolled study participants, variations in the dosing regimen and other clinical study parameters or the dropout rate among study participants. Product candidates in later stages of clinical studies often fail to demonstrate adequate safety and efficacy despite promising preclinical testing and earlier clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in later-stage clinical studies. Most product candidates that begin clinical studies are never approved for commercialization by regulatory authorities.

The reported results of our Phase 2 proof-of-concept trials of praliciguat in participants with diabetic nephropathy and in HFpEF are based on topline data. While we intend to follow our previously announced strategy not to continue internal development of praliciguat in diabetic nephropathy, we believe that positive trends on primary and secondary endpoints indicate a profile that merits further investigation. However, topline data may ultimately differ from actual results as additional evaluations are completed.

The reported results of our Phase 2 proof-of-concept trials of praliciguat in participants with diabetic nephropathy and in HFpEF that we have publicly disclosed, and that are discussed herein, consist of topline data. Topline data are based on a preliminary analysis of currently available efficacy and safety data, and therefore the reported results, findings and conclusions related to such clinical trials are subject to change following a comprehensive review of the more extensive data that we expect to receive related to these clinical trials. Topline data are based on important assumptions, estimations, calculations and information currently available to us. We continue to evaluate all data related to our Phase 2 proof-of-concept trials of praliciguat, including for one clinical trial site in the DN study where data was found to be inconsistent with the overall study population. Topline results may differ from future results, or different conclusions or considerations may qualify such results, as additional data is evaluated. In addition, third parties, including regulatory agencies and potential third-party licensees, may not accept or agree with our assumptions, estimations, calculations or analyses or may interpret or weigh the importance of data differently. If the topline data that we have reported related to our Phase 2 proof-of-concept trials of praliciguat differ from actual results, our ability to potentially obtain approval for or out-license and commercialize praliciguat may be harmed, which could harm our business, financial condition, operating results or prospects.

If we encounter difficulties in enrolling participants in our clinical studies, we could be delayed or prevented from proceeding with clinical trials of our product candidates.

Identifying and qualifying participants to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can

recruit participants to participate in testing our product candidates. Estimates of the prevalence of our target indication, SCD, vary considerably. Determining the incidence of these conditions, including in specific geographies or demographic groups, is challenging. The lower the actual prevalence of these conditions, the more challenges we will encounter enrolling participants in our clinical studies, which could delay development of our product candidates. Clinical trial enrollment may also encounter difficulties for a variety of other reasons. The number of participants eligible for a clinical trial may be substantially limited by stringent eligibility criteria in a study protocol, such as the inclusion of biomarker-driven identification or other highly specific criteria related to stage of disease progression or to specific patient reported outcome measures. The number of participants required to power the statistical analysis of the study's endpoints may be very large leading to an extended enrollment period. Issues such as the proximity of participants to a study site, the complexity of the study design, our ability to recruit investigators with appropriate skill and experience, competing clinical studies for similar therapies or targeting similar participants, perceptions of the benefit-risk profile of the product candidate relative to other available therapies or product candidates, and ability to obtain and maintain institutional review board, or IRB, or ethics committee, or EC, approvals and participant consents all could have a substantial impact on the timing of clinical trial enrollment. If we are unable to enroll sufficient participants in clinical studies in a timely way, obtaining study results will be delayed, which may harm our business, prospects, financial condition and results of operations.

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

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical studies and depends upon numerous factors, including the type and complexity of the product candidates involved. Regulatory authorities have substantial discretion in the approval process and may refuse to accept an application for review, or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. We have not requested or obtained regulatory approval for any product candidate, and 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 ongoing clinical studies may not be completed on schedule, and our planned clinical studies may not begin on schedule, if at all. The completion or commencement of clinical studies can be delayed or prevented for a number of reasons, including, among others:

- the FDA or other regulatory bodies may not authorize us or our investigators to commence planned clinical studies, or require that we suspend ongoing clinical studies through imposition of clinical holds;
- negative results from our ongoing studies or other industry studies involving product candidates modulating the same or similar mechanism of action;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites, the terms of which can be subject to considerable negotiation and may vary significantly among different CROs and study sites;
- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical studies, for example delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining EC or IRB approval to conduct a clinical study at a prospective site or sites;
- challenges in recruiting and enrolling participants to participate in clinical studies, the proximity of participants to study sites, eligibility criteria for the clinical study, the nature of the clinical study protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical study programs for similar indications;
- severe or unexpected drug-related side effects experienced by participants in a clinical study;
- the presence of unanticipated metabolites in participants in a clinical study may require considerable preclinical and clinical assessment;

- we may decide, or regulatory authorities may require us, to conduct additional clinical studies or abandon product development programs;
- delays in validating, or inability to validate, any endpoints utilized in a clinical study;
- the FDA or other regulatory bodies may disagree with our clinical study design and our interpretation of data from clinical studies, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical studies;
- reports from preclinical or clinical testing of other competing candidates that raise safety or efficacy concerns; and
- difficulties retaining participants who have enrolled in a clinical study but may be prone to withdraw due to rigors of the clinical studies, lack of efficacy, side effects, personal issues, or loss of interest.

Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical study may be suspended or terminated by us, the FDA or other comparable authorities, the IRBs or ECs overseeing a clinical study, a data and safety monitoring board overseeing the clinical study at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical study operations or study sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including in response to the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing studies, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue clinical studies.

Our product candidates may cause side effects that are presented in the product labeling approved by regulatory authorities. Some may result in label restrictions.

The most commonly reported adverse events in the clinical studies for olinciguat were headaches, tachycardia, dizziness, nausea, vomiting and hypotension. The most commonly reported adverse events in the clinical studies for praliciguat were respiratory infections, diarrhea nausea, and hypoglycemia. As with ADEMPAS® (riociguat), the only FDA-approved sGC stimulator to date, our product candidates include a warning on the possibility of serious birth defects if taken while pregnant. These side effects and any other undesirable side effects observed with our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in restrictive label language or delay or denial of regulatory approval.

Changes in regulatory requirements, FDA guidance or unanticipated events during our preclinical studies and clinical studies of our product candidates may occur, which may result in changes to preclinical or clinical study protocols or additional preclinical or clinical study requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or unanticipated events during our preclinical studies and clinical studies may force us to amend preclinical studies and clinical study protocols or the FDA may impose additional preclinical studies and clinical study requirements. Amendments or changes to our clinical study protocols would require resubmission to the FDA and IRBs for review and approval, which may increase the cost or delay the timing or successful completion of clinical studies. Similarly, amendments to our preclinical studies may increase the cost or delay the timing or successful completion of those preclinical studies. If we experience delays completing, or if we terminate, any of our preclinical or clinical studies, or if we are required to conduct additional preclinical or clinical studies, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or other comparable foreign regulatory authority grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical or clinical studies, as studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States, as well as other risks. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our product candidates is also subject to approval.

Obtaining non-U.S. regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such countries. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, prospects, financial condition and results of operations.

Data/market exclusivity may be more limited than we expect based upon the competitive landscape and other factors outside of our control that may occur during development or after approval.

There are many types of data/market exclusivity mechanisms that we have sought and continue to seek to secure. Many of these have risk of loss of exclusivity if the competitive landscape changes or regulations are revised. In June 2018, olinciguat received orphan drug designation for the treatment of patients with SCD in the US which confers additional exclusivity. If we seek and are awarded orphan drug designation in the EU based upon criteria in effect at the time, this designation may be rescinded if a similar drug or another therapy that confers a significant benefit over ours is subsequently approved. If olinciguat or our other product candidates were to fail to obtain orphan drug status, or lose such status after it is obtained, or the marketing exclusivity that such status provides, our business, prospects, financial condition and results of operations could be materially harmed. There are other types of data/ market exclusivity rights granted after approval that may not confer exclusivity anticipated if the competitive landscape changes and our business, prospects, financial condition and results of operations could be materially harmed.

Risks Related to Our Reliance on Third Parties

We may not succeed in our pursuit of an out-license agreement for the development and commercialization of praliciguat, which would materially adversely affect our financial condition and results of operations.

We are seeking an out-license of praliciguat for the purpose of pursuing further development and commercialization of praliciguat. There is no certainty that we will find a commercial or financial partner to fund and undertake development and commercialization, and failure to find such a partner may result in the discontinuation of development of praliciguat. We may also incur costs to wind down our activities related to this product candidate. Failure to find a partner for the continued development and commercialization of praliciguat would materially adversely affect our financial condition and results of operations.

Any collaboration or license arrangements that we enter into in the future may not be successful, which could impede our ability to develop and commercialize our product candidates.

We intend to seek collaboration or license arrangements for the commercialization, and/or potentially for the development, of certain of our product candidates depending on the merits of retaining

commercialization rights for ourselves as compared to entering into collaboration or license arrangements. We will face significant challenges in seeking appropriate partners. Moreover, collaboration and license arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement such arrangements. The terms of any collaborations, licenses or other arrangements that we may establish may not be favorable to us.

Any future collaboration or license arrangements that we enter into may not be successful. The success of such arrangements will depend heavily on the efforts and activities of our partners. Collaboration and license arrangements are subject to numerous risks, including that:

- partners have significant discretion in determining the efforts and resources that they will apply to collaborations;
- a partner with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- partners may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- collaboration and license arrangements may be terminated, and, if terminated, this may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- partners may own or co-own intellectual property covering products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaboration or license arrangements; and
- a partner's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

We rely, and expect that we will continue to rely, on third parties to conduct any preclinical or clinical studies for our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical studies. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct clinical studies on our product candidates. We rely heavily on such parties for execution of clinical studies for our product candidates and can control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical studies and the management of data developed through clinical studies than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may have staffing difficulties, fail to comply with contractual obligations, experience regulatory compliance issues, undergo changes in priorities, become financially distressed or form relationships with other entities, some of which may be our competitors.

These factors may materially impede the willingness or ability of third parties to complete quality clinical studies and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our clinical studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with regulations and guidelines, including good clinical practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical studies to ensure that the data and results are scientifically credible and accurate, and that the study participants are adequately informed of the potential risks of participating in clinical studies. These regulations are enforced by the FDA and comparable foreign regulatory authorities for any products

in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical study sponsors, principal investigators and study sites. If we and our CROs or our investigators fail to comply with applicable GCPs, the clinical data generated in our clinical studies may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical studies comply with GCPs. In addition, our clinical studies must be conducted with product candidates produced under current good manufacturing practice, or GMP, regulations and will require a large number of participants. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we design our product candidate clinical studies, CROs conduct all of the clinical studies. As a result, many important aspects of the execution of our drug development programs are outside of our direct control. In addition, the CROs may not perform all of their obligations under arrangements with us or in compliance with regulatory requirements, but we remain responsible and are subject to enforcement action that may include civil penalties and criminal prosecution for any violations of FDA laws and regulations during the conduct of our clinical studies. If the CROs do not perform clinical studies in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development and commercialization of our product candidates may be delayed or our development program materially and irreversibly harmed. We may fail to control the amount and timing of resources these CROs devote to our program or our clinical products. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of our clinical studies and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical studies such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the approved indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We rely completely on third-party suppliers to manufacture our non-clinical and clinical drug supplies for our product candidates, and we intend to rely on third parties to produce commercial supplies of any product candidates that are approved.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture the clinical drug supply of our product candidates, or any future product candidates, for use in the conduct of our clinical studies. We lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. We depend on third-party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our ongoing clinical trials of olinciguat and IW-6463. We do not have long-term supply agreements in place with our CMOs and each batch of our product candidates is individually contracted under a services agreement on a purchase order basis. We expect to continue to rely on CMOs for the supply of olinciguat and IW-6463 for later-stage development and commercialization, as well as for the supply of any other product candidates that we may identify, and we may not be able to enter into long-term supply agreements with such CMOs on favorable terms. As a further result, we are subject to price fluctuations for our clinical drug supplies. If the prices charged by these CMOs increase, our business, prospects, financial condition and results of operations could be materially harmed. We apply industry risk management practices to minimize the impact to clinical timelines associated with delays to our clinical supplies. However, these delays could still lead to clinical trials delays that could adversely impact our business.

In addition, the facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including current GMP,

after we submit our new drug application, or NDA, or relevant foreign regulatory submission to the applicable regulatory agency. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities are noncompliant, we may need to find alternative manufacturing facilities, which would impede our ability to develop, obtain regulatory approval for or market our product candidates.

Our reliance on third parties requires us to share our confidential information, including trade secrets and know-how, which increases the possibility that our confidential information will be misappropriated or disclosed.

Because we rely on third parties to manufacture our product candidates, and because we collaborate with various CROs to conduct our clinical trials, we must, at times, share our trade secrets or know-how with them. We seek to protect our confidential information, including know-how and trade secrets, in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors and consultants prior to beginning our collaborations or disclosing confidential information to such parties. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets and know-how. Despite these contractual provisions, the need to share our confidential information with third parties increases the risk that confidential information such as trade secrets and know-how becomes known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our confidential information including know-how and trade secrets, a competitor's discovery of our confidential information or other unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business, prospects, financial condition and results of operations.

Risks Related to Our Intellectual Property Rights

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

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection in the United States and other countries for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, should they issue, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business.

As of February 10, 2020, we had twelve issued U.S. patents, nineteen pending U.S. patents applications, six pending Patent Cooperation Treaty ("PCT") applications, and numerous foreign patents and pending patent applications. Our issued U.S. and foreign patents covering olinciguat expire between 2031 and 2034 and our issued U.S. and foreign patents covering praliciguat also expire between 2031 and 2034, in each case subject to patent term extensions. Multiple pending U.S. and foreign patents applications covering different aspects of olinciguat and praliciguat will expired between 2034 and 2040, subject to patent term extensions. We have one issued patents covering IW-6463, which expires in 2037, subject to patent term extensions. Our pending patent applications relating to IW-6463, if issued, will expire in 2037 or later. See "*Business — Intellectual Property*." We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent positions of biotechnology and pharmaceutical companies, including ours, involve complex legal and factual questions, which in recent years have been the subject of much litigation, and, therefore, the issuance, scope, validity, enforceability and commercial value of any patent claims that we may obtain cannot be predicted with certainty. Our pending patent applications may not be granted as issued patents in any particular jurisdiction and, even if they do, these patents may not include claims with a sufficient scope to protect our product candidates or otherwise provide any competitive advantage.

Even if our patent applications are issued, competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. We may not be able to prevent infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the attention of our management and key personnel from our business operations.

Moreover, our patents, if issued, may be challenged, deemed unenforceable, invalidated or circumvented in the United States and abroad. U.S. patents and patent applications may also be subject to interference, derivation, ex-parte reexamination, post-grant review, or inter-partes review proceedings, supplemental examination and challenges in district court. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our involvement in litigation or interference proceedings may fail and, even if successful, may result in substantial costs, and distract our management and other employees. Furthermore, an adverse decision in an interference or derivation proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates.

Patents may also be subjected to opposition, post-grant review or comparable proceedings lodged in various foreign, both national and regional, patent offices or courts. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. In addition, such proceedings may be costly. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors.

Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate protection to exclude competitors from making similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around or circumvent our patents, such as by using pre-existing or newly developed technology or products in a non-infringing manner. If these developments were to occur, they could have a material adverse effect on our business, prospects, financial condition and results of operations.

Any litigation to enforce or defend our patent rights, even if we were to prevail, would be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents, if and when issued, puts our patents at risk of being invalidated, held unenforceable or not infringed, or interpreted narrowly. Such proceedings could also provoke third parties to assert counterclaims against us, including that some or all of the claims in one or more of our patents are invalid, not infringed or unenforceable. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions of a patent include allegations that someone connected with prosecution of the patent application that matured into the patent withheld relevant information from the U.S. Patent and Trademark Office (the “USPTO”), or made a misleading statement, during prosecution of the patent application. In an infringement proceeding, a court may disagree with our allegations and refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question, or may decide that a patent of ours is invalid or unenforceable. An adverse result in any litigation, defense or post-grant proceedings could result in one or more of our patents being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it would have a material adverse effect on the price of our common stock.

The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, 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.

If any of our patents, if and when issued, covering our product candidates are invalidated or found not infringed or unenforceable, our business, prospects, financial condition and results of operations could be materially harmed.

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

Our success will depend in part on our ability to operate without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. Other parties may allege that our product candidates or the use of our technologies infringes or otherwise violates patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to compositions, materials, formulations, methods of manufacture or methods for treatment related to our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by our technologies.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain and cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either does not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license.

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

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

Our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors enter into confidentiality and intellectual property assignment agreements with us or have entered into confidentiality and intellectual property assignment agreements with Ironwood. We seek to have inventions assigned to us by the person rendering services. However, we may not be able to enter into these agreements with all parties or these agreements may not be honored and may not effectively assign intellectual property rights to us.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose

valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions over the lifetime of our owned patents and applications. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors or other third parties might be able to enter the market earlier than would otherwise have been the case and this circumstance could have a material adverse effect on our business, prospects, financial condition and results of operations.

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

The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications and we may not timely file foreign patent applications. Thus, for each of the patent families that we believe provide coverage for our product candidates, we will need to decide whether and where to pursue protection outside the United States. Filing and prosecuting patent applications, and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and so we are unlikely to pursue and maintain patents in all countries worldwide. As such, competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products.

The laws of some foreign countries may not protect intellectual property rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States even if we have a patent in that jurisdiction. Further, a competitor may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology or pharmaceuticals. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of or marketing of competing products in violation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our

efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we do not obtain additional protection under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business, prospects, financial condition and results of operations may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent term extension as compensation for patent term lost during the FDA regulatory review process. A maximum of five years can be restored to the eligible patent. In all cases, the total patent life for the product with the patent extension cannot exceed 14 years from the product's approval date, or in other words, 14 years of potential marketing time. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the duration of patent protection we obtain for our product candidates may not provide us with any meaningful commercial or competitive advantage, our competitors may obtain approval of competing products earlier than they would otherwise be able to do so, and our ability to generate revenues could be harmed.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act (the "America Invents Act"). The America Invents Act includes a number of significant changes to U.S. patent law. These provisions affect the way patent applications will be prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business, prospects, financial condition and results of operations.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

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

Our employees may have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities.

We may be subject to claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially harm our commercial development efforts.

Risks Related to the Future Commercialization of Our Product Candidates

The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate, or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability may be harmed.

The incidence and prevalence for all the conditions we aim to address with our programs vary considerably. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new trials may change the estimated incidence or prevalence of these diseases. The total addressable market across all of our product candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of our product candidates, if approved for sale for these indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products or new patients may become increasingly difficult to identify or gain access to, all of which would harm our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

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

We do not currently have an infrastructure for the sale, marketing, market access, patient service and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory authority outside the United States, we must build our sales, marketing, managerial and other non-technical capabilities, or arrange with third parties to perform these services. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time-consuming and could delay any product candidate launch. If commercialization is delayed or does not occur, we would have prematurely or unnecessarily incurred such expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

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

Even if we obtain regulatory approval for our product candidates, our product candidates may not achieve broad market acceptance by patients, physicians, healthcare payors or others in the medical community, which would limit the revenue that we generate from their sales.

The future commercial success of our product candidates, if approved by the FDA or other applicable regulatory authorities outside the United States, will depend upon the awareness and acceptance of our

product candidates among the medical community, including patients, physicians and healthcare payors. If any of our product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians, healthcare payors and others in the medical community, we may not generate sufficient revenue to become, or remain, profitable. Market acceptance of our product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy and safety of our approved product candidates as demonstrated in clinical trials;
- the clinical indications and labeling claims for our product candidates that are approved;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA or other applicable regulatory authorities;
- any restrictions on the use of our products together with other medications or restrictions on the use of our products in certain types of patients;
- the prevalence and severity of any adverse effects associated with our product candidates;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the safety, efficacy, cost and other potential advantages of our approved product candidates compared to other available therapies;
- our ability to generate cost effectiveness data that supports a profitable price;
- our ability to obtain sufficient reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of sufficient payor coverage;
- the effectiveness of our sales and marketing strategies; or
- publicity concerning our products or competing products and treatments.

If our product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably. Price controls may be imposed in certain markets, which may harm our future profitability.

Market acceptance and sales of any approved product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors and government authorities and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is: a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational.

Obtaining coverage and reimbursement 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 supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. We or our partners may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products. In addition, in the United States, third-party payors are increasingly attempting to

contain health care costs by limiting both coverage and the level of reimbursement of new drugs. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs.

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partners may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

If we fail to comply with healthcare and other regulations, we could face substantial penalties and our business, prospects, financial condition and results of operations could be harmed.

The product candidates that we are evaluating in clinical studies are subject to certain federal and state healthcare laws and regulations that may affect our business. These laws and regulations include:

- federal healthcare program anti-kickback laws, which prohibit, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, as an inducement or reward for their past, current or potential future prescribing, purchase, use, recommending for use, referral, formulary placement, or dispensing of our products;
- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product and medical device research, development, and marketing, prohibits manufacturers from marketing or promoting such products prior to approval; and
- state law equivalents of the above federal laws, such as anti-kickback laws, state transparency laws, state laws limiting interactions between pharmaceutical manufacturers and members of the healthcare industry and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

In addition, we may be subject to privacy and security laws in the various jurisdictions in which we operate, obtain or store personally identifiable information. For example, if we conduct clinical studies in any of the member states of the European Union, the processing of personal data in the European Economic Area (the “EEA”), is subject to the 1995 Data Protection Directive, imposing strict obligations and restrictions on the ability to collect, analyze and transfer personal data. In May 2018, the General Data Protection Regulation (the “GDPR”), took effect, increasing our obligations with respect to clinical studies conducted in the EEA and increasing the scrutiny applied by clinical study sites located in the EEA to transfers of personal data from such sites to countries that are considered by the European Commission to lack an adequate level of data protection, such as the United States. The compliance obligations imposed by the GDPR may increase our cost of doing business. In addition, the GDPR imposes substantial fines for breaches of data protection requirements, and it confers a private right of action on data subjects for breaches of data protection requirements.

If our operations are found to be in violation of any of the laws described above or any other laws, rules or regulations that apply to us, we will be subject to penalties, including civil and criminal penalties,

damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could impede our ability to operate our business and our financial results. We cannot be certain that compliance programs will address all areas of potential exposure and the risks in this area cannot be entirely eliminated, particularly because the requirements and government interpretations of the requirements in this space are constantly evolving. Any action against us for violation of these laws, rules or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business, as well as damage our business or reputation. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and reporting laws may prove costly.

We face significant competition in an environment of rapid technological and scientific change, and our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may harm our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of our product candidates. Our objective is to design, develop and commercialize new products with superior efficacy, safety, tolerability and convenience. In many cases, our product candidates that we commercialize will compete with existing, market-leading products. The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Bayer AG and Merck & Co., Inc. ("Bayer/Merck"), have an active collaboration on sGC and may be targeting some of the same indications through a similar mechanism of action with one sGC stimulator, ADEMPAS® (riociguat), which has been approved for the treatment of Pulmonary Arterial Hypertension, or PAH, and Chronic Thromboembolic Pulmonary Hypertension, or CTEPH. Bayer/Merck are also evaluating sGC product candidates in a number of indications, including vericiguat for the treatment of heart failure. Such sGC products may compete directly with our own product candidates in our target indications. Because Bayer/Merck already have experience conducting successful clinical trials and obtaining regulatory approvals for an sGC product, they may be able to conduct clinical trials and obtain regulatory approvals for additional product candidates and target indications more quickly or efficiently than we can.

Furthermore, we are aware of a number of other approved products and late-stage product candidates for the treatment of our target indications. In SCD, there are four approved products. Three drugs are indicated to reduce the frequency of painful crises, hydroxyurea (DROXIA® or SIKLOS®, as well as other generic forms) ENDARI®, an amino acid l-glutamine, and ADAKVEO® (crizanlizumab-tmca) a selectin blocker. Additionally, Oxbryta® (voxelotor), a hemoglobin S polymerization inhibitor, is indicated to treat sickle cell disease. We are aware of the following companies engaged in the clinical development of products for the chronic treatment of SCD: Novartis, which is developing ILARIS® (canakinumab) (Phase 2), a fully human monoclonal anti-human interleukin-1b antibody; AstraZeneca plc, which is developing ticagrelor (Phase 3), a P2Y12 platelet inhibitor in pediatric and adolescent patients; Micelle BioPharma, Inc., which is developing SC411 (Phase 3), a mixture of fatty acids; Imara, Inc., which is developing IMR-687 (Phase 2), a phosphodiesterase-9 inhibitor, or PDE9i; Shire/Takeda who are developing SHP655 (Phase 1/2), a recombinant ADAMTS13 von Willebrand factor-cleaving (VWF) protease, Agios, which is developing Mitapivat (Phase 1), a pyruvate kinase-R (PKR)activator, Forma Therapeutics which is developing FT-4202, a pyruvate kinase (PKR) activator (Phase 1), and Novo Nordisk which is developing an oral combination of tetrahydrouridine and decitabine (Phase 1). We are also aware of Prolong Pharmaceuticals, LLC which is developing Sanguinate (Phase 2), a PEGylated hemoglobin, for acute treatment in SCD. We may also face competition from one-time treatments such as HSCT, gene editing and gene therapy. We are aware of the following companies engaged in the clinical development of one-time treatments: bluebird bio, Inc. is currently conducting a Phase 1/2 study with their product, LentiGlobin®, for patients with severe SCD; and CRISPR Therapeutics AG/Vertex Pharmaceuticals, Inc. is conducting a Phase 1/2 study with their product,

CTX-001; and Bioverativ/Sangamo is conducting a Phase 1/2 study with their product, BIVV-003. There are several other companies engaged in earlier stage clinical development for products targeting SCD.

There are four approved products in the United States to treat DN. AVAPRO® (irbesartan) and COZAAR® (losartan), are an angiotensin II receptor blockers, indicated to treat DN in patients with type 2 diabetes mellitus and a history of hypertension. CAPOTEN® (captopril), angiotensin I converting enzyme inhibitor, indicated to reduce the rate of progression in patients with Type 1 insulin-dependent diabetes mellitus and retinopathy. INVOKANA®, is an SGLT2 inhibitor indicated to improve renal and cardiovascular outcomes in patients with diabetes mellitus and diabetic nephropathy. We are aware of the following companies engaged in the late-stage clinical development of products for the treatment of DN: AstraZeneca plc has a Phase 3 study ongoing with FARXIGA®, an SGLT2 inhibitor, assessing renal outcomes and cardiovascular mortality in patients with chronic kidney disease. Eli Lilly/Boehringer Ingelheim GmbH are currently conducting a Phase 3 program in DN with JARDIANCE. Bayer has a Phase 3 program ongoing for the investigational product finerenone, a mineralocorticoid receptor antagonist, assessing its effect in patients with DN. Bayer also has a Phase 2 program ongoing for BAY1142524, a chymase inhibitor, in patients with diabetic kidney disease. There are several other companies engaged in earlier stage clinical development for products targeting DN.

If our product candidates do not obtain regulatory approvals in our target indications prior to these or any other competing product candidates, or if our product candidates do not demonstrate superior efficacy, safety or tolerability compared to these and any other approved therapeutics for our target indications, we may not be able to compete effectively.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical studies, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. See "— *Risks Related to Our Intellectual Property Rights*."

The impact of healthcare reform and other governmental and private payor initiatives may harm our business.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to health care availability, the method of delivery or payment for health care products and services could harm our business, operations and financial condition. There is significant interest in promoting health care reform, as evidenced by the enactment in the United States of the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act in 2010. It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing health care legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect: the demand for any drug products for which we may obtain regulatory approval; our ability to set a price that we believe is fair for our products; our ability to obtain coverage and reimbursement approval for a product; our ability to generate revenues and achieve or maintain profitability; and the level of taxes that we are required to pay.

Our future growth may depend, in part, on our ability to commercialize our product candidates outside the United States, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates outside the United States for which we may rely on partnerships with third parties. If we commercialize our product candidates outside the United States, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates outside the United States;
- our ability to gain reimbursement in foreign markets at a price that is profitable;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be harmed by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

In light of the large population of patients with SCD who reside in foreign countries, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement limitations imposed by governments outside of the United States.

In some countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, or to meet other criteria for pricing approval. Given the significant portion of the population of patients with SCD who reside outside of the United States, if reimbursement of olinciguat, if approved, is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, prospects, financial condition and results of operations could be harmed.

If any of our product candidates obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or an ANDA, seeking approval of a generic copy of an approved, small-molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA that references the FDA's prior approval of the small-molecule innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug

Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or NDA applicant that seeks to market its product before expiration of the patents must include in the ANDA a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents.

Accordingly, if any of our product candidates are approved, competitors could file ANDAs for generic versions of our small-molecule drug products or NDAs that reference our small-molecule drug products, respectively. If there are patents listed for our small-molecule drug products in the Orange Book, those ANDAs and NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially.

Risks Related to Our Business Operations

A pandemic, epidemic or outbreak of infectious disease, such as COVID-19, has the potential to disrupt our business, including our clinical development activities, and its effect on our business is difficult to precisely judge at this time.

A novel strain of coronavirus (COVID-19) has reached pandemic levels. We are conducting multiple clinical development activities at various locations. Many nations, including the United States, have implemented stay-at-home orders to contain the coronavirus outbreak which, along with other related mitigation measures, may limit our ability to access patients and physicians at certain local clinical centers that are participating in these development activities. To a limited extent this has delayed or disrupted and may be expected to further delay or disrupt our clinical development activities. The extent to which this hinders procurement of resources, raw materials or components necessary for research studies or preclinical or clinical development is not fully predictable. New information is expected to emerge about the severity of the coronavirus and the actions to contain the coronavirus or treat its effects. To a limited extent we have experienced and may further experience other delays and disruptions, such as limitations on access to capital and to our personnel, resources and facilities or the temporary closure of our suppliers and suspension of services, which may materially and adversely affect our development timelines, results of operations and our financial condition.

Our prospects for success depend on our ability to retain our management team and to attract, retain and motivate qualified personnel.

We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer, Peter M. Hecht, Ph.D., our President, Mark Currie, Ph. D, our Chief Financial Officer, William Huyett, our Chief Innovation Officer, Andreas Busch, Ph.D. and our Head of Global Development, Christopher Wright, M.D., Ph.D. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors and an inability to find suitable replacements could result in delays in product development and harm our business. Pursuant to their employment arrangements, each of our executive officers, and other employees may voluntarily terminate their employment at any time, with or without notice. 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 competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against 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 may be able to offer. We also experience competition for the hiring of scientific personnel from universities and research institutions. The failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. In addition, in order to induce employees to continue their employment with us, we have provided equity awards that vest over time and the value to our employees of such equity awards may be significantly affected by movements in our stock price that are beyond our control and may be at any time insufficient to counteract more lucrative offers from other companies. 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.

We will need to expand our organization and we may experience difficulties in managing growth of our employee base, which could disrupt our operations.

As of December 31, 2019, we had 94 full-time employees. As we mature, we expect to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its 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, operational mistakes, 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 additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

The use of our product candidates in clinical studies and the sale of our products, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with our product candidates. For example, we may be sued if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things: withdrawal of subjects from our clinical studies; substantial monetary awards to patients or other claimants; decreased demand for our product candidates or any future product candidates following marketing approval, if obtained; damage to our reputation and exposure to adverse publicity; increased FDA warnings on product labels; litigation costs; distraction of management's attention from our primary business; loss of potential revenue; and the inability to successfully commercialize our product candidates or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical studies through both domestic and international insurance policies, subject to an annual coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer if a judgment or settlement exceeds available insurance proceeds. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be

substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our business, prospects, financial condition and results of operations could be materially harmed.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may or may not be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, if approved, or require us to suspend or abandon our commercialization efforts of any approved product candidates. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, prospects, financial condition and results of operations.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), and the rules and regulations of the Nasdaq Global Select Market. Until the Separation, our financial results were included within the consolidated results of Ironwood and we had not been directly subject to reporting and other requirements of the Exchange Act and Section 404 of the Sarbanes-Oxley Act. We are an "emerging growth company" and a "smaller reporting company." For so long as we remain an emerging growth company, we will be exempt from Section 404(b) of the Sarbanes-Oxley Act, which requires auditor attestation to the effectiveness of internal control over financial reporting. We will cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total gross annual revenues of $1.07 billion or more; (ii) December 31, 2024, the last day of our fiscal year following the fifth anniversary of the date of the distribution; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including exemption from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on the exemptions available to us as an emerging growth company and/or smaller reporting company. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We are, however, subject to Section 404(a) of the Sarbanes-Oxley Act. Beginning with our annual report on Form 10-K for the fiscal year ended December 31, 2020, we must include a management assessment of the effectiveness of our internal control over financial reporting. As of the expiration of our emerging growth company status and smaller reporting company status, we will be broadly subject to enhanced reporting and other requirements under the Exchange Act and Sarbanes-Oxley Act. This will require, among other things, annual management assessments of the effectiveness of our internal control over financial reporting and a report by our independent registered public accounting firm addressing these assessments. These and other obligations will place significant demands on our management, administrative and operational resources, including accounting and information technology resources. To comply with these requirements, we anticipate that we will need to further upgrade our systems, including duplicating computer hardware infrastructure, implement additional financial and management controls, reporting systems and procedures and hire additional accounting, finance and information technology staff. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costlier. If we are unable to do this in a timely and effective fashion, our ability to

comply with our financial reporting requirements and other rules that apply to reporting companies could be impaired and our business, prospects, financial condition and results of operations could be harmed.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities.

Unfavorable global economic conditions could harm our business, prospects, financial condition and results of operations.

Our results of operations could be harmed by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business, prospects, financial condition and results of operations.

Our internal computer systems, or those of our third-party CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs, CMOs, business development partners and other contractors and consultants may be vulnerable to damage from computer viruses, unauthorized access, ransomware, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical study data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Insurance may not be adequate to fully cover costs to restore data and resume normal working operations, which could harm our business, prospects, financial condition and results of operation.

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

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable foreign regulators, provide accurate information to the FDA and applicable foreign regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately and/or disclose unauthorized activities to us. In particular, research and development, commercialization and business arrangements in the healthcare industry are subject to considerable laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict, regulate or prohibit a wide range of activities pertaining to clinical trials including the informed consent process, data integrity and conducting the study in accordance with the investigational plan, and for approved products, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of,

including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions, possible exclusions from participation in Medicare, Medicaid and other U.S. federal healthcare programs, contractual damages and reputational harm.

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

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

We could be adversely affected by violations of the U.S. Foreign Corrupt Practices Act (the "FCPA"), and other worldwide anti-bribery laws.

We are subject to the FCPA, which prohibits U.S. corporations and their representatives from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Other countries have enacted similar anti-corruption laws and/or regulations. In some countries in which we operate, the pharmaceutical and life sciences industries are exposed to a high risk of corruption associated with the conduct of clinical trials and other interactions with healthcare professionals and institutions. Any such activities could expose us to potential liability under the FCPA, which may result in us incurring significant criminal and civil penalties and to potential liability under the anti-corruption laws and regulations of other jurisdictions in which we operate. In addition, the costs we may incur in defending against an FCPA investigation could be significant.

Risks Related to the Separation

We may not achieve some or all of the expected benefits of the Separation, and the separation could harm our business, prospects, financial condition and results of operations.

We may not be able to achieve some or all of the anticipated strategic, financial, operational, marketing or other benefits expected to result from the Separation, or such benefits may be delayed or not occur at all.

These actions may not provide the benefits we currently expect, and could lead to disruption of our operations, loss of or inability to recruit, key personnel needed to operate and grow our businesses, weakening of our internal standards, controls or procedures and impairment of our key collaborations and supplier relationships.

By separating from Ironwood, we may have become more susceptible to market fluctuations and other adverse events than we would have been if we were still a part of the Ironwood organizational structure. As part of Ironwood, we were able to benefit from Ironwood's experience and expertise as a commercial-stage company developing multiple products, and opportunities to pursue integrated strategies with Ironwood's other business activities. We also benefited from Ironwood's strategic advantages as an established market participant, including its improved negotiating power and historical partnerships. Additionally, when we were part of Ironwood, we benefited from Ironwood's market reputation, historical performance

and brand identity when operating our business. As a newly formed, independent, publicly traded company, we do not have, and may never develop, a comparable market reputation, performance or brand identity of our own, which may limit our ability to recruit and retain personnel, pursue and negotiate strategic transactions, and access the capital markets to finance our operations. If we fail to achieve some or all of the benefits that we expect to achieve as an independent company, or do not achieve them in the time we expect, our business, prospects, financial condition and results of operations may be materially harmed.

Our intellectual property license agreement with Ironwood could result in our being unable to use or delayed in using licensed know-how used in research and development, possibly requiring us to develop or acquire alternative know-how, which would involve cost and delay.

In connection with the Separation, we entered into an intellectual property license agreement with Ironwood, in connection with which Ironwood granted to us a license to use certain Ironwood know-how in connection with our research and development of sGC stimulator products. If we were to use such licensed know-how and if our rights under the intellectual property license agreement were challenged by a third party or we were otherwise prevented from exercising our rights as contemplated under the intellectual property license agreement, our research and development activities could be delayed until we were able to either resume exercising such rights or develop or acquire adequate alternative know-how, which would involve cost and delay.

Our historical financial information is not necessarily representative of the results that we would have achieved as a separate, publicly traded company and should not be relied upon as an indicator of our future results.

Certain of our historical combined information provided in this prospectus is derived from the consolidated financial statements and accounting records of Ironwood. Accordingly, the historical and combined financial information included in this prospectus may not reflect the operating results, financial condition or cash flows that we would have achieved as a separate, publicly traded company during the periods presented, or the financial results we will achieve in the future. In particular, our future financial results may vary from the historical and combined financial information included in this prospectus as a result of the following factors, among others:

- our historical combined financial data prior to the Separation does not reflect the Separation;
- our historical financial data prior to the Separation reflects expense allocations for certain business and support functions that are provided on a centralized basis within Ironwood, such as expenses for research and development and corporate administrative services, including information technology, finance, legal, insurance, compliance and human resources activities, that may be lower than the comparable expenses we would have actually incurred, or will incur in the future, as a standalone company;
- the Separation may have a material effect on our relationships with our suppliers, collaborators and other business relationships.

As a result of the Separation, it may be difficult for investors to compare our future results to historical results or to evaluate our relative performance or trends in our business.

If the Separation and distribution, together with certain related transactions, did not qualify as a transaction that was tax-free for U.S. federal income tax purposes, Ironwood could be subject to significant tax liabilities, and we could be required to indemnify Ironwood for all or a portion of such taxes and related costs pursuant to indemnification obligations under the tax matters agreement.

Ironwood received a favorable private letter ruling from the IRS relating to the U.S. federal income tax treatment of the distribution. Consistent with the IRS's ruling guidelines, the IRS private letter ruling did not cover all of the issues that are relevant to determining whether the distribution was generally tax free for U.S. federal income tax purposes. In addition, as a condition to the distribution, Ironwood received an opinion of KPMG LLP confirming that the distribution, together with certain related transactions, generally was tax-free for U.S. federal income tax purposes under Sections 355 and 368(a)(1)(D) of the Internal Revenue Code of 1986, as amended (the "Code"). The opinion of KPMG LLP delivered to Ironwood and the IRS private letter ruling are based, among other things, on various facts and assumptions, as well as

certain representations, statements and undertakings from us and Ironwood (including those relating to the past and future conduct of us and Ironwood). If any of these facts, assumptions, representations, statements or undertakings is, or becomes, inaccurate or incomplete, or if we or Ironwood breach any of our respective covenants relating to the Separation, the IRS private letter ruling and/or the opinion of KPMG LLP may be invalid. In addition, the opinion of KPMG LLP delivered to Ironwood represents the judgment of KPMG LLP, which is not binding on the IRS or any court. Accordingly, notwithstanding receipt by Ironwood of the tax opinion and the favorable IRS private letter ruling referred to above, the IRS could assert that the distribution and/or certain related transactions did not qualify for tax-free treatment for U.S. federal income tax purposes.

If the distribution, together with certain related transactions, failed to qualify as a transaction that was tax-free under Sections 355 and 368(a)(1)(D) of the Code, for U.S. federal income tax purposes, Ironwood would recognize taxable gain with respect to our distributed common stock and Ironwood stockholders who received shares of our common stock in the distribution would be subject to tax as if they had received a taxable distribution equal to the fair market value of such shares.

Even if the distribution otherwise qualified as tax-free for U.S. federal income tax purposes, under Sections 355 and 368(a)(1)(D) of the Code, Ironwood may have been required to recognize taxable gain under Section 355(e) of the Code as if it had sold our distributed shares for fair market value if the distribution were deemed to be part of a plan (or series of related transactions) pursuant to which one or more persons acquire, directly or indirectly, shares representing a 50% or greater interest (by vote or value) in Ironwood or us. Under the terms of the common stock purchase agreement, the investors in the private placement acquired 43% of our common stock on a basic shares outstanding method. For purposes of this test, the private placement will generally be treated as part of such a plan or series of transactions, although some portion of the private placement may have been excluded from such treatment if investors who owned shares of Ironwood common stock immediately prior to the distribution participated in the private placement to maintain their respective ownership held immediately prior to the private placement. The rules governing such exclusions are complex, and there can be no assurance given as to the amount or percentage of the private placement that will be excluded from such treatment under these rules. Thus, a relatively minor additional change in the ownership of the our common stock could trigger a prohibited change in control, resulting in a significant amount of taxable gain for Ironwood under Section 355 of the Code (as a result of which we would be required to indemnify Ironwood under the tax matters agreement, as discussed below), if that additional ownership change and the portion of the private placement that must be taken into account (together with, in certain circumstances, changes in ownership of Ironwood common stock) were each considered to be part of a plan or series of related transactions that included the distribution and, in the aggregate, resulted in a 50% or greater change in ownership of our common stock, as determined under the Code and applicable Treasury regulations. The process for determining whether a prohibited change in control has occurred under the rules is complex, inherently factual and subject to interpretation of the facts and circumstances of a particular case. If we or Ironwood do not carefully monitor our or its compliance with these rules, we or Ironwood might inadvertently cause or permit a prohibited change in our ownership or the ownership of Ironwood. Furthermore, sales and/or acquisitions by the investors in the private placement (or by other persons) of our or Ironwood common stock could potentially trigger a prohibited change of control in us or Ironwood. For purposes of these rules, any acquisitions of Ironwood or our shares within the period beginning two years before the distribution and ending two years after the distribution are presumed to be part of such a plan, although we or Ironwood may be able to rebut that presumption based on the facts or circumstances or under regulatory safe harbors.

In connection with the distribution, we entered into a tax matters agreement with Ironwood pursuant to which we are responsible for certain liabilities and obligations following the distribution. In general, under the terms of the tax matters agreement, if the distribution, together with certain related transactions, failed to qualify as a transaction that was generally tax-free, for U.S. federal income tax purposes, under Sections 355 and 368(a)(1)(D) of the Code, and if and to the extent that such failure results from a prohibited change of control in Ironwood under Section 355(e) of the Code or an acquisition of shares of Ironwood common stock or assets or certain actions by Ironwood, then Ironwood will bear any resulting taxes, interest, penalties and other costs. If and to the extent that such failure results from a prohibited change of control in us under Section 355(e) of the Code or an acquisition of our stock or assets or certain actions by us, then we will indemnify Ironwood for any resulting taxes, interest, penalties and other costs, including any reductions in

Ironwood's net operating loss carryforwards or other tax assets. If such failure does not result from a prohibited change of control in Ironwood or us under Section 355(e) of the Code and both we and Ironwood are responsible for such failure, liability will be shared according to relative fault. If neither we nor Ironwood is responsible for such failure, Ironwood will bear any resulting taxes, interest, penalties and other costs. Our indemnification obligations to Ironwood under the tax matters agreement is not limited in amount or subject to any cap. If we are required to pay any taxes or indemnify Ironwood under the circumstances set forth in the tax matters agreement, we may be subject to substantial liabilities. To the extent that the tax matters agreement requires Ironwood to bear any taxes, interest and penalties, Ironwood is required to indemnify us in the event that the IRS or another taxing authority asserts that we are jointly and severally liable as a result of our having been included in Ironwood's consolidated or combined tax returns prior to the Separation.

We may not be able to engage in attractive strategic or capital-raising transactions as a result of the Separation.

To preserve the tax-free treatment of the Separation and the distribution for U.S. federal income tax purposes, for the period ending two years after the distribution, we will be prohibited under the tax matters agreement, except in specific circumstances, from: (i) entering into or approving any transaction or series of transactions involving the acquisition of our outstanding or newly issued equity that, when combined with other changes in ownership of our capital stock, results in a change in ownership of 3% or more; (ii) liquidating or partially liquidating, or merging or consolidating (unless we are the survivor); (iii) making or changing any entity classification election; (iv) ceasing to be engaged in an active trade or business, or selling, transferring or disposing of 25% or more of the net or gross assets of any active trade or business; (v) amending any of our organizational documents or taking any action affecting the voting rights of our capital stock; or (vi) redeeming or otherwise repurchasing any of our outstanding stock or options, unless we receive an IRS private letter ruling or an unqualified opinion of a tax advisor, in form and substance satisfactory to Ironwood, to the effect that such action will not result in tax liability to Ironwood in connection with the Separation and distribution. In addition, we are prohibited, except in specific circumstances, from taking or failing to take any action that would be inconsistent with or cause to be untrue any statement, information, covenant or representation from us relating to the IRS private letter ruling and/or the opinion of KPMG LLP or would prevent the distribution and certain related transactions from qualifying as a transaction that was generally tax-free for U.S. federal income tax purposes under Sections 355 and 368(a)(1) (D) of the Code. These restrictions may limit for a period of time our ability to pursue certain strategic transactions, equity issuances or repurchases or other transactions that we may believe to be in the best interests of our shareholders or that might increase the value of our business.

In connection with the Separation, we assumed and agreed to indemnify Ironwood for certain liabilities. If we are required to make payments pursuant to these indemnities to Ironwood, we may need to divert cash to meet those obligations and our financial results could be harmed.

Pursuant to the Separation agreement and certain other agreements we entered into with Ironwood, we assumed and agreed to indemnify Ironwood for certain liabilities for uncapped amounts, which may include, among other items, associated defense costs, settlement amounts and judgments. Payments pursuant to these indemnities may be significant and could harm our business, particularly indemnities relating to our actions that could impact the tax-free nature of the distribution and certain related transactions as discussed in more detail above. Third parties could also seek to hold us responsible for any of the liabilities of the Ironwood business. Ironwood agreed to indemnify us for liabilities of the Ironwood business, but such indemnity from Ironwood may not be sufficient to protect us against the full amount of such liabilities, and Ironwood may not fully satisfy its indemnification obligations. Moreover, even if we ultimately succeed in recovering from Ironwood any amounts for which we are held liable, we may be temporarily required to bear these losses ourselves. Each of these risks could harm our business, prospects, financial condition and results of operations.

Our agreements with Ironwood may not reflect terms that would have resulted from negotiations with unaffiliated third parties.

The agreements related to the Separation, including, among others, the separation agreement, the employment matters agreement, the tax matters agreement, the intellectual property license agreement, the

transition services agreements and the development agreement, were negotiated in the context of the Separation while we were still controlled by Ironwood. Until the distribution occurred, Ironwood effectively had the sole and absolute discretion to determine and change the terms of the Separation, including the terms of any agreements between Ironwood and us and the establishment of the record date and distribution date. As a result, the provisions thereof may be unfavorable to us and may not reflect terms that would have resulted from negotiations between unaffiliated third parties.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may fluctuate widely and you could lose all or part of your investment in our common stock as a result.

Our common stock has a limited trading history and the market price has fluctuated widely, and may in the future fluctuate widely, depending upon many factors, some of which are beyond our control, including the following:

- a relatively low-volume trading market for our shares of common stock may result, which could cause trades of small blocks of shares to have a significant impact on the price of our shares of common stock;
- results and timing of preclinical studies and clinical studies of our product candidates;
- the commercial performance of our products, if approved, as well as the costs associated with such activities;
- results of clinical studies of our competitors' products;
- failure to adequately protect our trade secrets;
- our inability to raise additional capital and the terms on which we raise it;
- commencement or termination of any strategic partnership or licensing arrangement;
- regulatory developments with respect to our products or our competitors' products, including any developments, litigation or public concern about the safety of such products;
- announcements concerning product development results, including clinical trial results, the introduction of new products or intellectual property rights of us or others;
- actual or anticipated fluctuations in our financial condition and our quarterly and annual operating results;
- deviations in our operating results from any guidance we may provide or the estimates of securities analysts;
- additions and departures of key personnel;
- the passage of legislation or other regulatory developments affecting us or our industry;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other shareholders;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- announcement or expectation of additional financing efforts;
- publication of research reports by securities analysts about us or our competitors or our industry and speculation regarding our company or our stock price in the financial or scientific press or in online investor communities;
- changes in market conditions in the pharmaceutical and biotechnology sector; and
- changes in general market and economic conditions.

In addition, if the market for stocks in our industry or industries related to our industry, or the stock market in general, experiences a loss of investor confidence, the trading price of our common stock could

decline for reasons unrelated to our business, results of operations, financial condition and prospects. If any of the foregoing occurs, it could cause our stock price to fall and may expose us to lawsuits that, even if unsuccessful, could be costly to defend and a distraction to management.

The market price for our common stock is particularly volatile.

The market for our common stock is characterized by significant price volatility when compared to seasoned issuers, and we expect that our stock price will continue to be more volatile than those of a seasoned issuer. Several factors cause the volatility in our share price. We are a speculative or "risky" investment due to our short operating history, lack of revenues and the uncertain success (including of regulatory approval) of any of our product candidates. For example, on October 30, 2019, we announced that topline results from our Phase 2 proof-of-concept trials of praliciguat in patients with diabetic nephropathy and in HFpEF did not meet statistical significance on their respective primary endpoints. After this announcement, the market price of our common stock decreased substantially. As a consequence of this risk, more risk-averse investors may, under the fear of losing all or most of their investment in the event of further negative news or lack of progress, be more inclined to sell their shares of our common stock more quickly and at greater discounts than would be the case with the stock of a seasoned issuer. Plaintiffs have, in the past, initiated securities class action litigation against a company following periods of volatility in the market price of its securities. We may in the future be the target of such litigation. Securities litigation could result in substantial costs and liabilities and could divert management's attention and resources.

If securities or industry analysts fail to initiate or maintain coverage of our stock, publish a negative report or change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us, our business, our market or our competitors. If securities or industry analysts fail to initiate coverage of our stock, the lack of exposure to the market could cause our stock price or trading volume to decline. If any of the analysts who cover us or may cover us in the future publish a negative report or change their recommendation regarding our stock adversely, or provide more favorable relative recommendations about our competitors, our stock price would likely decline. If any analyst who covers us or may cover us in the future were to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We do not expect to pay any cash dividends for the foreseeable future.

We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

We have adopted anti-takeover provisions in our articles of organization and bylaws and are subject to provisions of Massachusetts law that may frustrate any attempt to remove or replace our current board of directors or to effect a change of control or other business combination involving our company.

Our articles of organization and bylaws and certain provisions of Massachusetts law may discourage certain types of transactions involving an actual or potential change of control of our company that might be beneficial to us or our security holders. For example, our bylaws grant our directors the right to adjourn any meetings of shareholders. Our board of directors also may issue shares of any class or series of preferred stock in the future without shareholder approval and upon such terms as our board of directors may determine. The rights of the holders of our common stock will be subject to, and may be harmed by, the rights of the holders of any class or series of preferred stock that may be issued in the future. Massachusetts state law also prohibits us from engaging in specified business combinations unless the combination is approved or consummated in a prescribed manner. These provisions, alone or together, could delay hostile takeovers and changes in control of our company or changes in our management.

Our articles of organization designate the state and federal courts located within the Commonwealth of Massachusetts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our shareholders, which could discourage lawsuits against us and our directors and officers.

Our restated articles of organization designate the state and federal courts located within the Commonwealth of Massachusetts as the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to us or our shareholders, creditors or other constituents, any action asserting a claim arising pursuant to any provision of the Massachusetts Business Corporation Act (the "MBCA"), or any action asserting a claim governed by the internal affairs doctrine, in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants. In additional, our articles of organization provide that unless our board of directors consents in writing to the selection of an alternative forum, the U.S. federal district courts shall be the exclusive forum for the resolutions of any complaint asserting a cause of action arising under the U.S. federal securities laws. This exclusive forum provision may limit the ability of our shareholders to bring a claim in a judicial forum that such shareholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against the company and our directors and officers. Alternatively, if a court outside of Massachusetts were to find this exclusive forum provision inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings described above, we may incur additional costs associated with resolving such matters in other jurisdictions, which could harm our business, prospects, financial condition and results of operations.

USE OF PROCEEDS

This prospectus relates to the offer and sale from time to time of up to an aggregate of 6,062,500 shares of common stock for the account of the selling stockholders referred to in this prospectus. We will not receive any of the proceeds from the sale of any shares of common stock offered by the selling stockholders under this prospectus. Any proceeds from the sale of shares of common stock under this prospectus will be received by the selling stockholders. However, we received proceeds of $24.25 million from our sale of the shares to the selling stockholders pursuant to the Purchase Agreement. These proceeds received from our sale of common stock to the selling stockholders under the Purchase Agreement will be used for working capital and general corporate purposes. Please see “Selling Stockholders.”

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and are subject to, and qualified in their entirety by, our restated articles of organization and our amended and restated bylaws, and applicable law.

As of July 31, 2020, our restated articles of organization authorize us to issue five hundred million (500,000,000) shares, consisting of four hundred million (400,000,000) shares of common stock and one hundred million (100,000,000) shares of preferred stock. Our board of directors, at any time or from time to time, may reclassify any unissued shares of any class or series of capital stock into one or more existing or new classes or series.

As of July 31, 2020, 33,920,210 shares of common stock were outstanding, along with (i) 7,666,348 options to purchase our common stock, and (ii) 474,923 restricted stock units. No shares of preferred stock were outstanding.

Common Stock

Each outstanding share of our common stock entitles its holder to one vote on all matters submitted to a vote of the holders of our common stock. The holders of our common stock have no cumulative voting rights. Subject to preferences that may apply to shares of preferred stock outstanding at the time, holders of shares of common stock are entitled to receive dividends out of assets legally available at the times and in the amounts as our board of directors may from time to time determine. The holders of our common stock do not have preemptive or other similar subscription rights to purchase any of our securities under the MBCA, or our restated articles of organization or amended and restated bylaws. Our common stock is neither convertible nor redeemable. Upon our liquidation, the holders of our common stock are entitled to receive pro rata our assets which are legally available for distribution, after payment of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

All the outstanding shares of our common stock are, and all shares of common stock offered, when issued and paid for, will be, validly issued, fully paid and non-assessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of any shares of our preferred stock.

Preferred Stock

Subject to limitations of the MBCA and our restated articles of organization and amended and restated bylaws, our board of directors may, without further action by our shareholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine the designations, powers, preferences, privileges and relative participating, optional or special rights, any or all of which may be greater than the rights of our common stock, as well as the qualifications, limitations or restrictions thereof, including:

- the number of shares constituting each class or series;
- voting rights;
- rights and terms of redemption, including sinking fund provisions;
- dividend rights and rates;
- terms concerning the distribution of assets;
- conversion or exchange terms;
- redemption prices and terms; and
- liquidation preferences.

We will specify the following terms relating to any class or series of preferred stock offered by us:

- the title and stated value of the preferred stock;

- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;
- voting rights, if any, of the preferred stock;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

All shares of preferred stock offered, when issued and paid for, will be validly issued, fully paid and non-assessable and will not have any preemptive or subscription rights.

Satisfaction of any dividend preferences of outstanding shares of preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of preferred stock may be entitled to receive a preference payment in the event of our liquidation before any payment is made to the holders of shares of our common stock.

Anti-Takeover Effects of Our Organizational Documents

Our restated articles of organization and amended and restated bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of our board of directors but which may have the effect of delaying, deferring or preventing a future takeover or change in control of us unless such takeover or change in control is approved by our board of directors. These provisions include:

- *Action by written consent; special meetings of shareholders*. Our restated articles of organization provide that shareholder action can be taken only at an annual or special meeting of shareholders or by the unanimous written consent of all shareholders in lieu of such a meeting. Our restated articles of organization and amended and restated bylaws also provide that, except as otherwise required by law, special meetings of the shareholders can only be called pursuant to a resolution adopted by a majority of our board of directors or holders of at least 40% of our then outstanding common stock. Except as described above, shareholders are not permitted to call a special meeting or to require our board of directors to call a special meeting.
- *Advance notice procedures*. Our amended and restated bylaws establish an advance notice procedure for shareholder proposals to be brought before an annual meeting of our shareholders, including

proposed nominations of persons for election to the board of directors. Shareholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a shareholder who was a shareholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the shareholder's intention to bring that business before the meeting. Although the bylaws do not give our board of directors the power to approve or disapprove shareholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of us.

- *Proxy Access*. Our amended and restated bylaws provides that a shareholder or a group of shareholders meeting certain conditions may nominate candidates for election as a director at an annual meeting of our shareholders using "proxy access" provisions. These provisions allow one or more shareholders (up to 20, collectively), owning at least 3% of our outstanding common stock continuously for at least three years, to nominate for election to our board of directors and to be included in our proxy materials up to the greater of two individuals or 20% of our board of directors, subject to the provisions to be included in our bylaws, including the provision of timely written notice to our Secretary.
- *Number of directors and filling vacancies; election of directors*. Our restated articles of organization provide that the number of directors is established by the board of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office. The ability of our board of directors to increase the number of directors and fill any vacancies may make it more difficult for our shareholders to change the composition of our board of directors. Our amended and restated bylaws provide that a majority of the votes properly cast for the election of a director shall effect such election unless there are more nominees than directorships, in which case a plurality standard shall apply.
- *Authorized but unissued shares*. Our authorized but unissued shares of common stock and preferred stock are available for future issuance without shareholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.
- *Board authority to issue preferred stock*. Our restated articles of organization provide that upon the affirmative vote of a majority of the total number of directors then in office, our board of directors, without shareholder approval, may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock and the market value of our common stock. Under certain circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management.
- *Exclusive forum*. Our restated articles of organization will require, to the fullest extent permitted by law, that derivative actions brought in the name of Cyclerion, actions against our directors, officers and employees for breach of a fiduciary duty and other similar actions may be brought only in specified courts in the Commonwealth of Massachusetts. Although we believe this provision benefits us by providing increased consistency in the application of Massachusetts law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. See "*Risk Factors — Our articles of organization designate the state and federal courts located within the Commonwealth of Massachusetts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our shareholders, which could discourage lawsuits against us and our directors and officers*."

Anti-Takeover Provisions under Massachusetts Law

Provisions Regarding Business Combinations

Cyclerion is subject to the provisions of Chapter 110F of the MBCA. In general, Chapter 110F prohibits a publicly held Massachusetts corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that the stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, five percent or more of the corporation's voting stock.

Under Chapter 110F, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 90% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by our board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Massachusetts corporation may "opt out" of these provisions with an express provision in its original articles of organization or an express provision in its articles of organization or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Provisions Regarding a Classified Board of Directors

Section 8.06(b) of the MBCA provides that, unless a company opts out of such provision, the terms of directors of a public Massachusetts company shall be staggered by dividing the directors into three groups, as nearly equal in number as possible, with only one group of directors being elected each year. We have opted out of this default requirement for a classified board of directors.

Pursuant to Section 8.06(c)(2) of the MBCA, however, our board of directors may unilaterally opt back into default requirements under Section 8.06(b) of the MBCA and become a classified board of directors without the approval of our stockholders. Sections 8.06(d) and (e) of the MBCA provide that when a board of directors is so classified, (i) stockholders may remove directors only for cause, (ii) the number of directors shall be fixed only by the vote of the board of directors, (iii) vacancies and newly created directorships shall be filled solely by the affirmative vote of a majority of the remaining directors and (iv) a decrease in the number of directors will not shorten the term of any incumbent director. If our board of directors opts into this classified structure in the future, these provisions are likely to increase the time required for stockholders to change the composition of our board of directors. For example, at least two annual meetings would generally be necessary for stockholders to effect a change in a majority of the members of our board of directors. As a result, the ability of our board of directors to adopt a classified structure in the future without the approval of our stockholders could have the effect of discouraging a potential acquirer from making a tender offer for a majority of the outstanding voting interest of our capital stock or otherwise attempting to obtain control of Cyclerion.

The Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CYCN."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. Its address is 250 Royall Street, Canton, Massachusetts 02021 and its telephone number is (800) 522-6645.

SELLING STOCKHOLDERS

This prospectus relates to the offer and sale from time to time by the selling stockholders identified below of up to an aggregate 6,062,500 shares of our common stock. The shares of our common stock issued and sold to the selling stockholders were offered and sold pursuant to the exemption from the registration requirements of the Securities Act afforded by Section 4(a)(2) of the Securities Act.

We do not know how long the selling stockholders will hold the shares before selling them or how many shares the selling stockholders will sell and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock registered under the registration statement of which this prospectus is a part.

The following table sets forth the maximum number of shares of our common stock to be sold by each selling stockholder. Except for the ownership of the shares of common stock and except as otherwise indicated, the selling stockholders have not had any material relationship with us within the past three years.

We prepared the table based on information provided to us by the respective selling stockholders. We have not sought to verify such information. Additionally, the selling stockholders may have sold or transferred some or all of its shares of our common stock in transactions exempt from the registration requirements of the Securities Act since the date on which the information in the table was provided to us. Other information about the selling stockholders may also change over time.

Except as otherwise indicated, each selling stockholder has sole voting and dispositive power with respect to such shares.

	Shares of Common Stock Beneficially Owned Prior to the Offering[1][2]	Shares of Common Stock Being Offered Hereby	Shares of Common Stock Beneficially Owned After Completion of the Offering[4]	
Name of Selling Stockholder	Number	Number	Number	Percent[3]
A. M. Pappas Life Science Ventures V, LP[5]	982,828	982,828	0	0%
PV V CEO Fund LP[6]	79,672	79,672	0	0%
Slate Path Master Fund LP[7]	6,196,063	5,000,000	1,196,063	3.5%

(1) Beneficial ownership is determined in accordance with Rule 13d-3 under the Exchange Act.

(2) Ownership prior to the offering consists of shares directly owned by the selling stockholder.

(3) Calculated based on 33,920,210 shares of our common stock outstanding on July 31, 2020.

(4) No selling stockholder is obligated to sell all or any portion of the shares of our common stock shown as offered by it. Accordingly, we cannot estimate the actual number or percentage of shares of our common stock that will be held by any selling stockholder upon completion of this offering. However, for purposes of this table, we have assumed that all shares of common stock being registered under the registration statement of which this prospectus forms a part are sold in this offering, and that no selling stockholder acquires additional shares of our common stock after the date of this prospectus and prior to completion of this offering.

(5) The sole general partner of A.M. Pappas Life Science Ventures V, LP (“Pappas Ventures V”) is AMP&A Management V, LLC (“Management V”), which has a management services agreement with Pappas Capital, LLC (formerly A.M. Pappas & Associates, LLC) (“Pappas Capital”) whereby Pappas Capital provides management services for Pappas Ventures V. As a result, Pappas Capital’s investment committee exercises sole dispositive and voting power over the securities owned by Pappas Ventures V. Arthur M. Pappas is a manager of Management V and the sole managing member of Pappas Capital. By virtue of these relationships, Management V, Pappas Capital and Mr. Pappas may be deemed to beneficially own the securities owned directly by Pappas Ventures V. Each of Management V, Pappas Capital and Mr. Pappas disclaims beneficial ownership of such securities except to the extent of its or his respective pecuniary interest therein.

(6) The sole general partner of PV V CEO Fund LP (“PV V”) is Management V, which has a management services agreement with Pappas Capital whereby Pappas Capital provides management services for PV V. As a result, Pappas Capital’s investment committee exercises sole dispositive and voting power over the securities owned by PV V. Arthur M. Pappas is a manager of Management V and the sole

managing member of Pappas Capital. By virtue of these relationships, Management V, Pappas Capital and Mr. Pappas may be deemed to beneficially own the securities owned directly by PV V. Each of Management V, Pappas Capital and Mr. Pappas disclaims beneficial ownership of such securities except to the extent of its or his respective pecuniary interest therein.

(7) Slate Path Capital LP (the "Investment Manager"), a Delaware limited partnership acts as the investment manager of Slate Path Master Fund LP. Mr. David Greenspan serves as the managing member of Jades GP, LLC, a Delaware limited liability company and the general partner of the Investment Manager. Each of Slate Path Master Fund LP, the Investment Manager, Jades GP, LLC and Mr. David Greenspan expressly disclaims beneficial ownership of these securities.

In connection with the sale of the shares being offered hereby, we entered into a Purchase Agreement with the selling stockholders. The registration statement of which this prospectus forms a part has been filed in accordance with the Purchase Agreement.

PLAN OF DISTRIBUTION

The shares of common stock listed in the table appearing under “Selling Stockholders” are being registered to permit the resale of the shares by the selling stockholders from time to time after the date of this prospectus. There can be no assurance that the selling stockholders will sell any or all of the common stock offered hereby. We will not receive any of the proceeds from the sale of the common stock by the selling stockholders. We will pay substantially all of the expenses incident to this offering of the shares by the selling stockholders to the public other than commissions and discounts of underwriters, brokers, dealers or agents.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly to purchasers or through one or more underwriters, broker-dealers or agents, at market prices prevailing at the time of sale, at prices related to such market prices, at a fixed price or prices subject to change or at negotiated prices, by a variety of methods including the following:

- on any national securities exchange or over-the-counter market on which the shares of common stock may be listed or quoted at the time of sale;
- in the over-the-counter market;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which a broker-dealer may attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer, as principal, and a subsequent resale by the broker-dealer for its account;
- in “at the market” offerings to or through market makers into an existing market for the shares;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- sales pursuant to Rule 144;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- in transactions otherwise than on such exchanges or in the over-the-counter market;
- through a combination of any such methods; or
- through any other method permitted under applicable law.

In addition, the selling stockholders may enter into option, derivative or hedging transactions with respect to the shares, and any related offers or sales of shares may be made pursuant to this prospectus. For example, the selling stockholders may:

- enter into transactions involving short sales of the shares by broker-dealers in the course of hedging the positions they assume with selling stockholder;
- sell shares short itself and deliver the shares registered hereby to settle such short sales or to close out stock loans incurred in connection with their short positions;
- write call options, put options or other derivative instruments (including exchange-traded options or privately negotiated options) with respect to the shares, or which they settle through delivery of the shares;
- enter into option transactions or other types of transactions that require the selling stockholders to deliver shares to a broker, dealer or other financial institution, who may then resell or transfer the shares under this prospectus; or

- lend or pledge the shares to a broker, dealer or other financial institution, which may sell the shares under this prospectus.

In effecting sales, brokers-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate. If the selling stockholders effect such transactions by selling the common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the common stock for whom they may act as agent or to whom they may sell as principal. Underwriters may sell securities to or through dealers, and dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agent.

The selling stockholders may pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any underwriters, brokers, dealers or agents that participate in such distribution may be deemed to be “underwriters” within the meaning of the Securities Act, and any discounts, commissions or concessions received by any underwriters, brokers, dealers or agents might be deemed to be underwriting discounts and commissions under the Securities Act. Any selling stockholder who is an “underwriter” within the meaning of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act and the provisions of the Exchange Act and the rules thereunder relating to stock manipulation.

In order to comply with the securities laws of some states, the shares sold in those jurisdictions may only be sold through registered or licensed brokers or dealers. In addition, in some states, the shares may not be sold unless the shares have been registered or qualified for sale in that state or an exemption from registration or qualification is available and is complied with.

Underwriters, dealers and agents who participate in the distribution of securities and their controlling persons may be entitled, under agreements that may be entered into with us, to indemnification by us and the selling stockholders against certain liabilities, including liabilities under the Securities Act, or to contribution with respect to payments that the underwriters, dealers or agents and their controlling persons may be required to make in respect of those liabilities.

Once sold under the registration statement of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference information into this document. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act made subsequent to the date of this prospectus until the termination of the offering of the securities described in this prospectus (other than information in such filings that was "furnished," under applicable SEC rules, rather than "filed").

We incorporate by reference the following documents or information that we have filed with the SEC:

- our annual report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 12, 2020;
- our quarterly reports on Form 10-Q for the quarters ended March 31 and June 30, 2020, filed with the SEC on May 4 and August 3, 2020, respectively;
- our current reports on Form 8-K filed with the SEC on March 5, 2020, April 14, 2020 (only with respect to Item 8.01 thereof) and June 18, 2020 (only with respect to Item 5.07 thereof); and
- our definitive proxy statement on Schedule 14A filed with the SEC on April 23, 2020.

Any statement contained in this prospectus or contained in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any subsequently filed supplement to this prospectus, or document deemed to be incorporated by reference into this prospectus, modifies or supersedes such statement.

You may request a copy of these filings at no cost, by writing or telephoning us at the following address:

Cyclerion Therapeutics, Inc.
301 Binney Street
Cambridge, Massachusetts, 02142
(857) 327-8778
E-mail: IR@cyclerion.com

You should rely only on the information incorporated by reference or provided in this prospectus or in any prospectus supplement. We have not authorized anyone else to provide you with different or additional information. An offer of these securities is not being made in any jurisdiction where the offer or sale is not permitted. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference in this prospectus. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public from commercial document retrieval services and over the Internet at the SEC's website at http://www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at https://www.cyclerion.com/. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus.

LEGAL MATTERS

The validity of the shares offered hereby will be passed upon for us by Foley Hoag LLP, Boston, Massachusetts.

EXPERTS

The consolidated and combined financial statements of Cyclerion Therapeutics, Inc. as of December 31, 2019 and 2018, and for each of the years in the two-year period ended December 31, 2019, appearing in Cyclerion Therapeutics, Inc.'s annual report on Form 10-K, dated March 12, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the SEC) given on the authority of such firm as experts in accounting and auditing.

6,062,500 Shares of Common Stock

PROSPECTUS