

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

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

CYCLERION THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Massachusetts
(State or other jurisdiction of
incorporation or organization)

83-1895370
(I.R.S. Employer
Identification No.)

**301 Binney Street
Cambridge, Massachusetts, 02142
(857) 327-8778**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**William Huyett
Chief Financial Officer
301 Binney Street
Cambridge, Massachusetts, 02142
(857) 327-8778**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:

**Gary J. Simon, Esq.
Hughes Hubbard & Reed LLP
One Battery Park Plaza
New York, NY 10004
Telephone: (212) 837-6000**

**Approximate date of commencement of proposed sale to the public:
From time to time after the effective date of this registration statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box:

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box:

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

CALCULATION OF REGISTRATION FEE

Title of each class of Securities to be registered	Amount to be registered ⁽¹⁾	Proposed maximum offering price per unit ⁽²⁾	Proposed maximum aggregate offering price ⁽²⁾	Amount of registration fee
Common stock, with no par value per share ⁽³⁾				
Preferred stock, with no par value per share ⁽³⁾				
Debt securities ⁽³⁾				
Warrants ⁽³⁾				
Units ⁽³⁾				
Total:	\$150,000,000⁽⁴⁾		\$150,000,000	\$19,470

- (1) There are being registered hereunder such indeterminate number of common stock and preferred stock, debt securities, warrants and/or units of the registrant as shall have an aggregate initial offering price not to exceed \$150,000,000. Any securities registered hereunder may be sold separately or in combination with other securities registered hereunder. The proposed maximum offering price of the securities will be determined, from time to time, by the registrant in connection with the issuance by the registrant of the securities registered hereunder. The securities registered also include such indeterminate amounts and numbers of common stock as may be issued upon conversion of or exchange for preferred stock, debt securities, warrants or units that provide for such conversion or exchange. The amount of each class of securities being registered under this registration statement is not specified pursuant to General Instruction II.D. of Form S-3 under the Securities Act of 1933, as amended (the "Securities Act").
- (2) The proposed maximum aggregate offering price has been estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act. A filing fee of \$19,470 is being paid in connection with the filing of this registration statement.
- (3) Pursuant to Rule 416 under the Securities Act, an indeterminate number of additional securities are registered hereunder that may be issued to prevent dilution in connection with a stock split, stock dividend, recapitalization, or similar event or adjustment. In addition, an indeterminate number of shares of common stock are registered hereunder that may be issued upon conversion of or exchange for any convertible preferred stock or debt securities, or upon exercise of any warrant.
- (4) In no event will the aggregate initial offering price of all securities issued from time to time by the registrant pursuant to this registration statement exceed \$150,000,000 or the equivalent thereof in one or more foreign currencies, foreign currency units or composite currencies, excluding accrued interest, if any, on any debt securities issued under the registration statement.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

SUBJECT TO COMPLETION, DATED JULY 24, 2020

PROSPECTUS

\$150,000,000

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.



**Common Stock
Preferred Stock
Debt Securities**

Warrants Units

We may from time to time offer, in one or more series or classes, separately or together, and in amounts, at prices and on terms to be set forth in one or more supplements to this prospectus, the following securities:

- shares of our common stock, with no par value per share;
- shares of our preferred stock (which we may issue in one or more series), with no par value per share;
- debt securities;
- warrants to purchase shares of common stock or preferred stock or debt securities; or
- units consisting of two or more of the foregoing.

We refer to the common stock, preferred stock, debt securities, warrants and units, collectively, as the “securities” in this prospectus. We may offer, issue and sell the securities at an aggregate public offering price that will not exceed \$75,000,000.

We will provide the specific amount, price and terms of any securities we may offer in one or more supplements to this prospectus. You should carefully read this prospectus and the applicable prospectus supplement, as well as the documents incorporated or deemed to be incorporated by reference in this prospectus, before you purchase any of the securities offered hereby. This prospectus may not be used to offer and sell any securities unless accompanied by a prospectus supplement describing the amount of securities being offered and the terms of the offering of those securities.

We may offer and sell these securities to or through one or more underwriters, dealers, and agents, or directly to purchasers on a continuous or delayed basis. We reserve the sole right to accept, and together with any underwriters, dealers and agents, reserve the right to reject, in whole or in part, any proposed purchase of securities. The names of any underwriters, dealers or agents involved in the sale of any securities, the specific manner in which they may be offered and any applicable commissions or discounts will be set forth in the prospectus supplement covering the sale of those securities.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “CYCN.” On July 23, 2020, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$3.64.

As of July 23, 2020, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$98,677,958, which was calculated based on 27,109,329 shares of outstanding common stock held by non-affiliates and a price per share of \$3.64.

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 _____, 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, we may, over time, offer and sell any combination of the securities described in this prospectus in one or more offerings, up to a total dollar amount of \$150,000,000. This prospectus provides you with a general description of the securities that may be offered. 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.

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 “*Where You Can Find More Information*” and “*Information Incorporated by Reference*” 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 Pharmaceuticals, 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.
- *Praliciquat*. Praliciquat 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. Praliciquat 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 praliciquat 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 praliciquat treatment arms had undetectable or very low praliciquat 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 praliciquat 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 Cycleron 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.”

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, pralicyguat, 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 pralicyguat 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 pralicyguat in participants with HFpEF. However, there was a trend towards improvement across the total intention-to-treat diabetic nephropathy study population and pralicyguat was generally well tolerated, therefore, as previously announced, we intend to pursue an out-license of pralicyguat. 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 pralicyguat 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 pralicyguat 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 pralicyguat 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 pralicyguat, 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 pralicyguat differ from actual results, our ability to potentially obtain approval for or out-license and commercialize pralicyguat 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 praliguat 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 praliguat, which would materially adversely affect our financial condition and results of operations.

We are seeking an out-license of praliguat for the purpose of pursuing further development and commercialization of praliguat. 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 praliguat 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 addition, 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

Unless otherwise indicated in any prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, including clinical trial expenses, research and development expenses, general and administrative expenses, and potential partnerships with or acquisitions of companies and acquisitions or licensing of technologies.

DESCRIPTION OF SECURITIES WE MAY OFFER

This prospectus contains a summary description of the common stock, preferred stock, debt securities, warrants and units that we may offer from time to time. As further described in this prospectus, these summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the accompanying prospectus supplement and other offering material. The accompanying prospectus supplement may update, change or add to the terms and conditions of the securities as described in this prospectus.

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 23, 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 23, 2020, 27,857,710 shares of common stock were outstanding, along with (i) 7,666,465 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 nonassessable. 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 nonassessable 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 Cyclorion, 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.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities under one or more trust indentures to be executed by us and a specified trustee. The terms of the debt securities will include those stated in the indenture and those made a part of the indenture by reference to the Trust Indenture Act of 1939 (the “Trust Indenture Act”). The indentures will be qualified under the Trust Indenture Act.

The following description sets forth certain anticipated general terms and provisions of the debt securities to which an accompanying prospectus supplement may relate. The particular terms of the debt securities offered by an accompanying prospectus supplement (which terms may be different than those stated below) and the extent, if any, to which such general provisions may apply to the debt securities so offered will be described in the prospectus supplement relating to such debt securities. Accordingly, for a description of the terms of a particular issue of debt securities, investors should review both the accompanying prospectus supplement relating thereto and the following description. A form of the indenture (as discussed herein) has been filed as an exhibit to the registration statement of which this prospectus is a part.

The debt securities will be our direct obligations and may be either senior debt securities or subordinated debt securities. The indebtedness represented by subordinated securities will be subordinated in right of payment to the prior payment in full of our senior debt (as defined in the applicable indenture).

Except as set forth in the applicable indenture and described in an accompanying prospectus supplement relating thereto, the debt securities may be issued without limit as to aggregate principal amount, in one or more series, secured or unsecured, in each case as established from time to time in or pursuant to authority granted by a resolution of the board of trustees or as established in the applicable indenture. All debt securities of one series need not be issued at the same time and, unless otherwise provided, a series may be reopened, without the consent of the holders of the debt securities of such series, for issuance of additional debt securities of such series.

The accompanying prospectus supplement relating to any series of debt securities being offered will contain their specific terms, including, without limitation:

- their title and whether they are senior securities or subordinated securities;
- their initial aggregate principal amount and any limit on their aggregate principal amount;
- the percentage of the principal amount at which they will be issued and, if other than 100% of the principal amount, the portion of the principal amount payable upon declaration of acceleration of their maturity;
- the terms, if any, upon which they may be convertible or exchangeable into our common stock, other securities or other property and the terms and conditions upon which a conversion or exchange will be effected, including the initial conversion or exchange price or rate and the conversion or exchange period, any adjustments to the foregoing and any requirements relative to the reservation of shares for purposes of conversion or exchange;
- if convertible or exchangeable, any applicable limitations on the ownership or transferability of the common stock or preferred stock into which they are convertible or exchangeable;
- the date or dates, or the method for determining the date or dates, on which the principal will be payable;
- the rate or rates (which may be fixed or variable), or the method for determining the rate or rates, at which they will bear interest, if any;
- the date or dates, or the method for determining the date or dates, from which any interest will accrue, the interest payment dates on which any interest will be payable, the regular record dates for the interest payment dates, or the method by which the date will be determined and the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;
- the place or places where the principal (and premium, if any) and interest, if any, will be payable, or the method of such payment, if by wire transfer, mail or other means;

- the period or periods within which, the price or prices at which and the terms and conditions upon which they may be redeemed, as a whole or in part, at our option, if we are to have the option;
- our obligation, if any, to redeem, repay or purchase them pursuant to any sinking fund or analogous provision or at the option of a holder, and the period or periods within which, the price or prices at which and the terms and conditions upon which they will be redeemed, repaid or purchased, as a whole or in part, pursuant to this obligation;
- if other than U.S. dollars, the currency or currencies in which they are denominated and in which any payments of principal (and premium, if any) or interest, if any, are payable, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies, and the related terms and conditions;
- whether the payments of principal (and premium, if any) or interest, if any, may be determined with reference to an index, formula or other method (which index, formula or method may, but need not be, based on a currency, currencies, currency unit or units or composite currencies) and the manner in which the amounts will be determined;
- any additions to, modifications of or deletions from their terms with respect to the events of default, to the rights of the trustee or the holders to declare the principal amount thereof due and payable, or to the covenants, in each case as set forth in the indenture;
- any provisions for collateral security for their repayment;
- any provisions relating to guarantees;
- any trustees, depositories, interest rate calculation agents, exchange rate calculation agents or other agents;
- whether they will be issued in certificated or book-entry form;
- the date any temporary global security will be dated if other than the date of original issuance of the first security of such series to be issued;
- if issued in definitive form only upon receipt of certain certificates or other documents or satisfaction of other conditions, the form and/or terms of such certificates, documents or conditions;
- if to be issued upon the exercise of debt warrants, the time, manner and place to be authenticated and delivered;
- the denominations if other than \$1,000 and any integral multiple thereof;
- the applicability, if any, of defeasance and covenant defeasance provisions of the applicable indenture;
- whether and under what circumstances we will pay additional amounts as contemplated in the applicable indenture in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem them in lieu of making the payment; and
- any other terms and any deletions from or modifications or additions to the applicable indenture.

The debt securities may provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity thereof. Special federal income tax, accounting and other considerations applicable to debt securities will be described in the accompanying prospectus supplement.

The applicable indenture may contain provisions that would limit our ability to incur indebtedness or that would afford holders of debt securities protection in the event of a highly leveraged or similar transaction involving us or in the event of a change of control. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Neither the MBCA nor our governing instruments define the term “substantially all” as it relates to the sale of assets. Additionally, Massachusetts cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially

all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

Investors should review the accompanying prospectus supplement for information with respect to any deletions from, modifications of or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Merger, Consolidation or Sale

The applicable indenture will provide that we may consolidate with or merge into, or sell, convey, transfer or lease all or substantially all of our assets to any other person (as defined therein), provided that:

- we are the continuing entity, or the successor entity (if other than the Company) formed by or resulting from any consolidation or merger or which has received the transfer of our assets will be organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the applicable debt securities and under the indenture;
- immediately after giving effect to the transaction, no event of default under the applicable indenture, and no event which, after notice or the lapse of time, or both, would become an event of default, will have occurred and be continuing; and
- an officer’s certificate and legal opinion covering these conditions will be delivered to the trustee.

Covenants

The applicable indenture will contain covenants requiring us to take certain actions and prohibiting us from taking certain actions. The covenants with respect to any series of debt securities will be described in the accompanying prospectus supplement.

Events of Default, Notice and Waiver

Each indenture will describe specific “events of default” with respect to a series of debt securities issued under the indenture. These “events of default” are likely to include (with grace and cure periods):

- our failure to pay any installment of interest;
- our failure to pay the principal (or premium, if any) at maturity;
- our failure to make any required sinking fund payment;
- our breach of any other covenant or warranty contained in the applicable indenture (other than a covenant added to the indenture solely for the benefit of a different series of debt securities); and
- certain events of bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us or any substantial part of our property.

If an event of default resulting from certain events of bankruptcy described in the indenture occurs, all outstanding debt securities of that series will become due and payable immediately. If any other event of default under any indenture with respect to debt securities of any series at the time outstanding occurs and is continuing, then the applicable trustee or the holders of not less than 25% of the principal amount of the outstanding debt securities of that series may declare the principal amount (or, if the debt securities of that series are original issue discount securities or indexed securities, such portion of the principal amount as may be specified in the terms thereof) of all the debt securities of that series to be due and payable immediately by written notice thereof to us (and to the applicable trustee if given by the holders). However, at any time after such a declaration of acceleration with respect to debt securities of such series (or of all debt securities then outstanding under any indenture, as the case may be) has been made, the holders of not less than a majority in principal amount of outstanding debt securities of such series (or of all debt securities then outstanding under the applicable indenture, as the case may be) may rescind and annul such declaration and its consequences if:

- the rescission would not conflict with any judgment or decree; and

- all events of default, other than the non-payment of accelerated principal, interest or premium (or specified portion thereof), with respect to debt securities of such series (or of all debt securities then outstanding under the applicable indenture, as the case may be) have been cured or waived as provided in such indenture.

Each indenture also will provide that the holders of not less than a majority in principal amount of the outstanding debt securities of any series (or of all debt securities then outstanding under the applicable indenture, as the case may be) may waive any past default with respect to the series and its consequences, except a:

- continuing payment default; or
- covenant default that cannot be modified or amended without the consent of the holder of each outstanding debt security affected thereby.

Each trustee will be required to give notice to the holders of debt securities within a certain number of days of a default under the applicable indenture unless the default has been cured or waived; provided, however, that the trustee may withhold notice to the holders of any series of debt securities of any default with respect to the series (except a default in the payment of the principal of (or premium, if any) or interest on any debt security of the series or in the payment of any sinking fund installment in respect of any debt security of the series) if specified responsible officers of the trustee consider withholding the notice to be in the interest of the holders.

Each indenture will prohibit the holders of debt securities of any series from instituting any proceedings, judicial or otherwise, with respect to the indenture or for any remedy thereunder, except in the case of failure of the applicable trustee, for a certain period of time after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of not less than a majority in principal amount of the outstanding debt securities of such series, as well as the furnishing of indemnity reasonably satisfactory to it.

This provision will not prevent any holder of debt securities from instituting a suit to enforce the payment of the principal of (and premium, if any) and interest on the debt securities at the respective due dates thereof.

Subject to the indenture, no trustee will be under any obligation to exercise any of its rights or powers under an indenture at the request or direction of any holders of any series of debt securities then outstanding, unless the holders furnish the trustee thereunder reasonable security or indemnity. The holders of not less than a majority in principal amount of the outstanding debt securities of any series (or of all debt securities then outstanding under an indenture, as the case may be) will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon the trustee. However, a trustee may refuse to follow any direction, which is in conflict with any law or the applicable indenture, which may involve the trustee in personal liability or which may be unduly prejudicial to the holders of debt securities of such series not joining therein.

Within a certain period of time of the close of each fiscal year, we will be required to deliver to each trustee, a certificate, signed by one of several specified officers, stating whether or not the officer has knowledge of any default under the applicable indenture and, if so, specifying each default and the nature and status thereof.

Modification of the Indenture

The indenture will likely provide that it may be modified or amended, with the consent of the holders of not less than a majority in principal amount of each series of the outstanding debt securities issued under the indenture affected by the modification or amendment, provided that no modification or amendment may, without the consent of each affected holder of the debt securities:

- change the stated maturity date or reduce the amount of the principal of (or premium, if any) or reduce the rate of interest or change the time for payment of any installment of interest, if any, on the debt securities;

- change the currency of payment of principal of (or premium, if any) or interest, if any, on the debt securities;
- waive a default or event of default in the payment of principal of (or premium, if any) or interest on the debt securities (other than as described in the indenture);
- waive a redemption payment, if any, or alter or waive any of the provisions in the indenture with respect to redemption;
- reduce the above-stated percentage of holders of the debt securities necessary to modify or amend the indenture; or
- modify the foregoing requirements or reduce the percentage of the outstanding debt securities necessary to waive compliance with certain provisions of the indenture or for waiver of certain defaults.

A record date may be set for any act of the holders with respect to consenting to any amendment.

The holders of not less than a majority in principal amount of the outstanding debt securities of each series affected thereby will have the right to waive our compliance with certain covenants in the indenture. Each indenture will contain provisions for convening meetings of the holders of debt securities of a series to take permitted action. Under certain circumstances, we and the trustee may make modifications and amendments to an indenture without the consent of any holders of outstanding debt securities.

Conversion of Debt Securities

The terms and conditions, if any, upon which any debt securities are convertible or into our common stock or preferred stock will be set forth in the applicable accompanying prospectus supplement. The terms will include:

- whether the debt securities are convertible into our common stock or preferred stock;
- the conversion price (or the manner of calculating the price);
- the conversion period;
- the events requiring an adjustment to the conversion price and provisions affecting conversion if the debt securities are redeemed; and
- any restrictions on conversion.

Subordination

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated securities will be subordinated to the extent provided in the applicable indenture to the prior payment in full of all senior securities. No payment of principal or interest will be permitted to be made on subordinated securities at any time if any payment default or any other default which permits accelerations exists. After all senior securities are paid in full and until the subordinated securities are paid in full, holders of subordinated securities will be subrogated to the right of holders of senior securities to the extent that distributions otherwise payable to holders of subordinated securities have been applied to the payment of senior securities. By reason of any subordination, in the event of a distribution of assets upon our insolvency, some of our general creditors may recover more, ratably, than holders of subordinated securities. The accompanying prospectus supplement or the information incorporated herein by reference will contain the approximate amount of senior securities outstanding as of the end of our most recent fiscal quarter.

Global Debt Securities

The debt securities of a series may be issued in whole or in part in global form. The global securities will be deposited with a depository, or with a nominee for a depository, identified in the accompanying prospectus supplement. In this case, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding debt securities

of the series to be represented by the global security or securities. Unless and until it is exchanged in whole or in part for debt securities in definitive form, a global security may not be transferred except as a whole by the depository for the global security to a nominee of the depository or by a nominee of the depository to the depository or another nominee of the depository or by the depository or any nominee to a successor of the depository or a nominee of the successor.

The specific material terms of the depository arrangement with respect to any portion of a series of debt securities to be represented by a global security will be described in the applicable accompanying prospectus supplement. We anticipate that the following provisions will apply to all depository arrangements.

Upon the issuance of a global security, the depository for the global security will credit, on its book-entry registration and transfer system, the respective principal amounts of the debt securities represented by the global security to the accounts of persons or participants that have accounts with the depository. The accounts to be credited will be designated by any underwriters or agents participating in the distribution of the debt securities. Ownership of beneficial interests in a global security will be limited to participants or persons that may hold interests through participants. Ownership of beneficial interests in the global security will be shown on, and the transfer of that ownership will be effected only through, records maintained by the depository for the global security, with respect to interests of participants, or by participants or persons that hold through participants, with respect to interests of persons other than participants. So long as the depository for a global security, or its nominee, is the registered owner of the global security, the depository or the nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the global security for all purposes under the indenture; provided, however, that for purposes of obtaining any consents or directions required to be given by the holders of the debt securities, we, the trustee and our agents will treat a person as the holder of the principal amount of debt securities as specified in a written statement of the depository. Except as set forth herein or otherwise provided in the accompanying prospectus supplement, owners of beneficial interests in a global security will not be entitled to have the debt securities represented by the global security registered in their names, will not receive physical delivery of the debt securities in definitive form and will not be considered the owners or holders thereof under the indenture.

Principal, premium, if any, and interest payments on debt securities represented by a global security registered in the name of a depository or its nominee will be made to the depository or its nominee, as the case may be, as the registered owner of the global security. Neither we, the trustee nor any paying agent for the debt securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depository for any debt securities represented by a global security, upon receipt of any payment of principal, premium, if any, or interest will immediately credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the principal amount of the global security as shown on the records of the depository. We also expect that payments by participants will be governed by standing instructions and customary practices, as is now the case with the securities held for the accounts of customers registered in "street names" and will be the responsibility of the participants.

If the depository for any debt securities represented by a global security is at any time unwilling or unable to continue as depository and a successor depository is not appointed by us within the period of time set forth in the indenture, we will issue the debt securities in definitive form in exchange for the global security. In addition, we may at any time, and in our sole discretion, determine not to have any of the debt securities of a series represented by one or more global securities and, in that event, will issue debt securities of the series in definitive form in exchange for all of the global security or securities representing the debt securities.

The laws of some states require that certain purchasers of securities take physical delivery of the securities in definitive form. These laws may impair the ability to transfer beneficial interests in debt securities represented by global securities.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the Commonwealth of Massachusetts.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock, preferred stock or debt securities, and may issue warrants independently or together with common stock, preferred stock or debt securities, or attached to, or separate from, such securities. We will issue each series of warrants under a separate warrant agreement between us and a bank or trust company as warrant agent, as specified in the applicable prospectus supplement. The form of the warrant agreement and the form of the warrant certificate will be filed with the SEC and incorporated by reference as an exhibit to the registration statement of which this prospectus is a part.

The warrant agent will act solely as our agent in connection with the warrants and will not act for or on behalf of warrant holders. The following sets forth certain general terms and provisions of the warrants that may be offered under this registration statement. Further terms of the warrants and the applicable warrant agreement will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of the warrants in respect of which this prospectus is being delivered, including, where applicable, the following:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the type and number of securities purchasable upon exercise of such warrants;
- the designation and terms of the other securities, if any, with which such warrants are issued and the number of such warrants issued with each such offered security;
- the date, if any, on and after which such warrants and the related securities will be separately transferable;
- the price at which each security purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;
- the minimum or maximum amount of such warrants which may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- any anti-dilution protection;
- a discussion of certain U.S. federal income tax considerations; and
- any other terms of such warrants, including terms, procedures and limitations relating to the transferability, exercise and exchange of such warrants.

Warrant certificates will be exchangeable for new warrant certificates of different denominations and warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Prior to the exercise of their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise or to any dividend payments or voting rights as to which holders of the shares of common stock or preferred stock purchasable upon such exercise may be entitled.

Each warrant will entitle the holder to purchase for cash such number of shares of common stock, preferred stock or debt securities, at such exercise price as shall, in each case, be set forth in, or be determinable as set forth in, the applicable prospectus supplement relating to the warrants offered thereby. After the expiration date set forth in the applicable prospectus supplement, unexercised warrants will be void.

Warrants may be exercised as set forth in the applicable prospectus supplement relating to the warrants.

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the securities purchasable upon such exercise. If less than all of the warrants are presented for exercise with respect to a warrant certificate, a new warrant certificate will be issued for the remaining amount of warrants.

DESCRIPTION OF UNITS

We may issue units consisting of one or more of the other securities that may be offered under this prospectus, in any combination. Units may also include debt obligations of a third party. These units may be issuable as, and for a specified period of time may be transferable only as, a single security, rather than as the separate constituent securities comprising such units. The statements made in this section relating to the units are summaries only and are not complete. When we issue units, we will provide the specific terms of the units in a prospectus supplement. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

When we issue units, we will provide in a prospectus supplement the following terms of the units being issued when applicable:

- the title of any series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- information with respect to any book-entry procedures;
- a discussion of any material or special U.S. federal income tax consequences applicable to an investment in the units; and
- any other material terms of the units and their constituent securities.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, at the market offerings, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Unless stated otherwise in the applicable prospectus supplement, the obligations of any underwriter to purchase securities will be subject to certain conditions, and the underwriter will be obligated to purchase all of the applicable securities if any are purchased. If a dealer is used in a sale, we may sell the securities to the dealer as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

We or our agents may solicit offers to purchase securities from time to time. Unless stated otherwise in the applicable prospectus supplement, any agent will be acting on a best efforts basis for the period of its appointment.

In connection with the sale of securities, underwriters or agents may receive compensation (in the form of discounts, concessions or commissions) from us or from purchasers of securities for whom they may act as agents. Underwriters may sell securities to or through dealers, and such 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 agents. Underwriters, dealers and agents that participate in the distribution of securities may be deemed to be underwriters, as that term is defined in the Securities Act, and any discounts or commissions received by them from us and any profits on the resale of the securities by them may be deemed to be underwriting discounts and commissions under the Securities Act. We will identify any such underwriter or agent, and we will describe any compensation paid to them, in the related prospectus supplement.

Underwriters, dealers and agents may be entitled under agreements with us to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act.

If stated in the applicable prospectus supplement, we will authorize agents and underwriters to solicit offers by certain specified institutions or other persons to purchase securities at the public offering price set forth in the prospectus supplement under delayed delivery contracts providing for payment and delivery on a specified date in the future. Institutions with whom these contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions, and other institutions, but shall in all cases be subject to our approval. These contracts will be subject only to those conditions set forth in the applicable prospectus supplement and the applicable prospectus supplement will set forth the commission payable for solicitation of these contracts. The obligations of any purchaser under any such contract will be subject to the condition that the purchase of the securities shall not be prohibited at the time of delivery under the laws of the jurisdiction to which the purchaser is subject. The underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

The securities may or may not be listed on a national securities exchange or traded in the over-the-counter market, as set forth in the applicable prospectus supplement. No assurance can be given as to the liquidity of the trading market for any of our securities. Any underwriter may make a market in these securities. However, no underwriter will be obligated to do so, and any underwriter may discontinue any market making at any time, without prior notice.

If underwriters or dealers are used in the sale, until the distribution of the securities is completed, SEC rules may limit the ability of any underwriters and selling group members to bid for and purchase the

securities. As an exception to these rules, representatives of any underwriters are permitted to engage in certain transactions that stabilize the price of the securities. These transactions may consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities. If the underwriters create a short position in the applicable securities in connection with any offering (in other words, if they sell more securities than are set forth on the cover page of the applicable prospectus supplement) the representatives of the underwriters may reduce that short position by purchasing securities in the open market. The representatives of the underwriters may also elect to reduce any short position by exercising all or part of any over-allotment option we may grant to the underwriters, as described in the prospectus supplement. The representatives of the underwriters may also impose a penalty bid on certain underwriters and selling group members. This means that if the representatives purchase securities in the open market to reduce the underwriters' short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from the underwriters and selling group members who sold those shares as part of the offering.

In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of those purchases. The imposition of a penalty bid might also have an effect on the price of the securities to the extent that it discourages resales of the securities. The transactions described above may have the effect of causing the price of the securities to be higher than it would otherwise be. If commenced, the representatives of the underwriters may discontinue any of the transactions at any time. In addition, the representatives of any underwriters may determine not to engage in those transactions or that those transactions, once commenced, may be discontinued without notice.

Certain of the underwriters or agents and their associates may engage in transactions with and perform services for us or our affiliates in the ordinary course of their respective businesses.

In no event will the commission or discount received by any Financial Industry Regulatory Authority ("FINRA"), member or independent broker-dealer participating in a distribution of securities exceed 8% of the aggregate principal amount of the offering of securities in which that FINRA member or independent broker-dealer participates.

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 report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on May 4, 2020; 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 debt securities, warrants and units we may offer will be passed upon for us by Hughes Hubbard & Reed LLP, New York, New York and the validity of the common stock and preferred stock we may offer will be passed upon for us by Foley Hoag LLP, Boston, Massachusetts.

EXPERTS

The consolidated and combined financial statements of Cycleron 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 Cycleron 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.



Common Stock
Preferred Stock
Debt Securities
Warrants
Units

PROSPECTUS



PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the sale and distribution of the securities being registered. All of the amounts shown are estimates:

	<u>Amount to be paid</u>
SEC registration fee	\$ 19,470
FINRA filing fees	\$ 23,000
Printing expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Miscellaneous	*
Total	<u>\$ *</u>

* These fees are calculated based on the number of issuances and the amount of securities offered and accordingly cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers.

Indemnification of Directors and Officers

Our restated articles of organization provide that the liability of our directors for damages for any breach of fiduciary duty shall be limited to the fullest extent permitted by law. Our amended and restated bylaws provide that Cyclerion will indemnify, and advance funds to and reimburse expenses of, our directors and officers that have been appointed by our board of directors to the fullest extent permitted by law, and that we may indemnify, and advance funds to and reimburse expenses of, such other officers and employees as determined by our board of directors. The right of indemnification provided under our amended and restated bylaws is in addition to and not exclusive of any other rights to which any of our directors, officers or any other persons may otherwise be lawfully entitled. We entered into indemnification agreements with our directors and officers, and we carry insurance policies insuring our directors and officers against certain liabilities that they may incur in their capacity as directors and officers.

Cyclerion is incorporated under the laws of the Commonwealth of Massachusetts, and is governed by the MBCA. Part 8 of the MBCA authorizes the provisions, described above, that are contained in our restated articles of organization and amended and restated bylaws. In addition, Sections 8.30 and 8.42 of the MBCA provide that if an officer or director discharges his or her duties in good faith and with the care that a person in a like position would reasonably exercise under similar circumstances and in a manner the officer or director reasonably believes to be in the best interests of the corporation, he or she will not be liable for such action.

Item 16. Exhibits.

The list of exhibits following the signature page of this registration statement is incorporated by reference herein.

Item 17. Undertakings.

- (1) The undersigned registrant hereby undertakes:
- a. To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

- i. To include any prospectus required by Section 10(a)(3) of the Securities Act;
- ii. To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
- iii. To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that the undertaking set forth in paragraphs (1)(a)(i), (1)(a)(ii) and (1)(a)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act, that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

- b. That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; and
- c. To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- d. That, for the purpose of determining liability under the Securities Act to any purchaser:
 - i. Each prospectus filed by a registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - ii. Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- e. That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant hereby undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration

- statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- i. Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - ii. Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - iii. The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - iv. Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (2) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (3) The undersigned registrant hereby undertakes that:
- i. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance on Rule 430A and contained in a form of prospectus filed by the undersigned registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective; and
 - ii. For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (4) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.
- (5) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the undersigned registrant, pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the undersigned registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
1.1+	Form of Underwriting Agreement.
2.1	Separation Agreement, dated March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cycleron Therapeutics, Inc. (incorporated by reference to Exhibit 2.1 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787)).
3.1	Restated Articles of Organization of Cycleron Therapeutics, Inc. (incorporated by reference to Exhibit 4.1 to Registration Statement on Form S-8 filed on March 29, 2019) (File No. 333-230615).
3.2	Amended and Restated Bylaws of Cycleron Therapeutics, Inc. (incorporated by reference to Exhibit 4.2 to Registration Statement on Form S-8 filed on March 29, 2019) (File No. 333-230615).
4.1	Form of Indenture for debt securities between the Cycleron Therapeutics, Inc. and the trustee to be named therein.
4.2+	Form of Warrant Agreement and Warrant Certificate.
4.3+	Form of Unit Agreement.
5.1	Opinion of Hughes Hubbard & Reed LLP.
5.2	Opinion of Foley Hoag LLP.
23.1	Consent of Ernst & Young LLP.
23.2	Consent of Hughes Hubbard & Reed LLP (included as part of Exhibit 5.1).
23.3	Consent of Foley Hoag LLP (included as part of Exhibit 5.2).
24.1	Power of Attorney (included in the signature page to this registration statement).
25.1*	Statement of Eligibility of Trustee under the Indenture.

+ To be filed, if applicable, by amendment or as an exhibit to a document to be incorporated by reference or deemed to be incorporated by reference in this registration statement, including a Current Report on Form 8-K.

* To be filed separately in accordance with Section 305(b)(2) of the Trust Indenture Act of 1939, as amended, and the appropriate rules and regulations thereunder.

Cyclerion Therapeutics, Inc.,

Issuer

AND

Trustee

INDENTURE

Dated as of _____, 202_

TABLE OF CONTENTS*
CROSS-REFERENCE TABLE*

Section of Trust Indenture Act of 1939, as amended	Section of Indenture
310(a)	7.9
310(b)	7.8
310(c)	Inapplicable
311(a)	7.13
311(b)	7.13
311(c)	Inapplicable
312(a)	5.01, 5.02(a)
312(b)	5.2(c)
312(c)	5.2(c)
313(a)	5.4(a)
313(b)	5.4(b)
313(c)	5.4(b)
313(d)	5.4(c)
314(a)	5.3(a)
314(b)	Inapplicable
314(c)	13.7(a)
314(d)	Inapplicable
314(e)	13.7(b)
314(f)	Inapplicable
315(a)	7.1(b)
315(b)	7.14
315(c)	7.1(a)
315(d)	7.1(b)
315(e)	6.7
316(a)	6.6, 8.4
316(b)	6.4
316(c)	8.1
317(a)	6.2
317(b)	4.3
318(a)	13.9
318(c)	13.9

*This Cross-Reference Table does not constitute part of the Indenture and shall not have any bearing on the interpretation of any of its terms or provisions.

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*This Table of Contents does not constitute part of the Indenture and shall not have any bearing upon the interpretation of any of its terms or provisions.

INDENTURE, dated as of _____, 202__, among Cycleron Therapeutics, Inc., a Massachusetts corporation (the “Company”), and _____, as trustee (the “Trustee”):

WHEREAS, for its lawful corporate purposes, the Company has duly authorized the execution and delivery of this Indenture to provide for the issuance of unsecured debt securities (hereinafter referred to as the “Securities”), in an unlimited aggregate principal amount to be issued from time to time in one or more series as in this Indenture provided, as registered Securities without coupons, to be authenticated by the certificate of the Trustee;

WHEREAS, to provide the terms and conditions upon which the Securities are to be authenticated, issued and delivered, the Company has duly authorized the execution of this Indenture; and

WHEREAS, all things necessary to make this Indenture a valid agreement of the Company, in accordance with its terms, have been done.

NOW, THEREFORE, in consideration of the premises and the purchase of the Securities by the holders thereof, it is mutually covenanted and agreed as follows for the equal and ratable benefit of the holders of Securities:

ARTICLE I DEFINITIONS

Section 1.1 Definitions of Terms.

The terms defined in this Section 1.1 (except as herein otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section 1.1 and shall include the plural as well as the singular. All other terms used in this Indenture that are defined in the Trust Indenture Act of 1939, as amended, or that are by reference therein defined in the Securities Act of 1933, as amended (except as herein otherwise expressly provided or unless the context otherwise requires), shall have the meanings assigned to such terms in said Trust Indenture Act and in said Securities Act as in force at the date of the execution of this instrument.

“**Affiliate**” means, with respect to a specified Person, (a) any Person directly or indirectly owning, controlling or holding with power to vote 10% or more of the outstanding voting securities or other ownership interests of the specified Person, (b) any Person 10% or more of whose outstanding voting securities or other ownership interests are directly or indirectly owned, controlled or held with power to vote by the specified Person, (c) any Person directly or indirectly controlling, controlled by, or under common control with the specified Person, (d) a partnership in which the specified Person is a general partner, (e) any officer or director of the specified Person, and (f) if the specified Person is an individual, any entity of which the specified Person is an officer, director or general partner.

“**Authenticating Agent**” means an authenticating agent with respect to all or any of the series of Securities appointed with respect to all or any series of the Securities by the Trustee pursuant to Section 2.10.

“**Bankruptcy Law**” means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors.

“**Board of Directors**” means the Board of Directors of the Company or any duly authorized committee of such Board.

“**Board Resolution**” means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company to have been duly adopted by the Board of Directors and to be in full force and effect on the date of such certification.

“**Business Day**” means, with respect to any series of Securities, any day other than a day on which Federal or State banking institutions in the City of New York or place of payment, are authorized or obligated by law, executive order or regulation to close.

“**Certificate**” means a certificate signed by the principal executive officer, the principal financial officer, the Treasurer or the principal accounting officer of the Company. The Certificate need not comply with the provisions of Section 13.7.

“**Company**” means Cycleron Therapeutics, Inc., a corporation, duly organized and existing under the laws of the Commonwealth of Massachusetts and, subject to the provisions of Article Ten, shall also include its successors and assigns.

“**Corporate Trust Office**” means the office of the Trustee at which, at any particular time, its corporate trust business shall be principally administered, which office at the date hereof is located at _____.

“**Custodian**” means any receiver, trustee, assignee, liquidator, or similar official under any Bankruptcy Law.

“**Default**” means any event, act or condition that with notice or lapse of time, or both, would constitute an Event of Default.

“**Defaulted Interest**” has the meaning set forth in Section 2.3 hereof.

“**Depository**” means, with respect to Securities of any series, for which the Company shall determine that such Securities will be issued as a Global Security, The Depository Trust Company, New York, New York, another clearing agency, or any successor registered as a clearing agency under the Exchange Act, or other applicable statute or regulation, which, in each case, shall be designated by the Company pursuant to either Section 2.1 or 2.11.

“**Event of Default**” means, with respect to Securities of a particular series any event specified in Section 6.1, continued for the period of time, if any, therein designated.

“**Exchange Act**” means the Securities and Exchange Act of 1934, as amended.

“Global Security” means, with respect to any series of Securities, a Security executed by the Company and delivered by the Trustee to the Depository or pursuant to the Depository’s instruction, all in accordance with the Indenture, which shall be registered in the name of the Depository or its nominee.

“Governmental Obligations” means securities that are (i) direct obligations of the United States of America for the payment of which its full faith and credit is pledged or (ii) obligations of a Person controlled or supervised by and acting as an agency or instrumentality of the United States of America, the payment of which is unconditionally guaranteed as a full faith and credit obligation by the United States of America that, in either case, are not callable or redeemable at the option of the issuer thereof, and shall also include a depositary receipt issued by a bank (as defined in Section 3(a)(2) of the Securities Act) as custodian with respect to any such Governmental Obligation or a specific payment of principal of or interest on any such Governmental Obligation held by such custodian for the account of the holder of such depositary receipt; provided, however, that (except as required by law) such custodian is not authorized to make any deduction from the amount payable to the holder of such depositary receipt from any amount received by the custodian in respect of the Governmental Obligation or the specific payment of principal of or interest on the Governmental Obligation evidenced by such depositary receipt.

“Guarantee” means any obligation, contingent or otherwise, of any Person directly or indirectly guaranteeing any indebtedness of any other Person and any obligation, direct or indirect, contingent or otherwise, of such Person (a) to purchase or pay (or advance or supply funds for the purchase or payment of) such indebtedness or other obligation of such Person (whether arising by virtue of partnership arrangements, or by agreements to keep-well, to purchase assets, goods, securities or services, to take-or-pay or to maintain financial statement conditions or otherwise) or (b) entered into for the purpose of assuring in any other manner the obligee of such indebtedness of the payment thereof or to protect such obligee against loss in respect thereof (in whole or in part); provided, however, that the term “Guarantee” shall not include endorsements for collection or deposit in the ordinary course of business. The term “Guarantee” used as a verb has a corresponding meaning.

“Guarantor” means any Person Guaranteeing any obligation.

“Guaranty Agreement” means a supplemental indenture, in a form satisfactory to the Trustee, pursuant to which a Person Guarantees the Company’s obligations with respect to a series of Securities.

“herein”, **“hereof”** and **“hereunder”**, and other words of similar import, refer to this Indenture as a whole and not to any particular Article, Section or other subdivision.

“Indenture” means this instrument as originally executed or as it may from time to time be supplemented or amended by one or more indentures supplemental hereto entered into in accordance with the terms hereof.

“Interest” when used with respect to an Original Issue Discount Security which by its terms bears interest only after maturity, means interest payable after maturity.

“Interest Payment Date”, when used with respect to any installment of interest on a Security of a particular series, means the date specified in such Security or in a Board Resolution or in an indenture supplemental hereto with respect to such series as the fixed date on which an installment of interest with respect to Securities of that series is due and payable.

“Officer” means the Chairman of the Board, the Chief Executive Officer, the President, any Executive Vice President, any Vice President, the Treasurer, the Secretary or an Assistant Secretary of the Company.

“Officers’ Certificate” means a certificate signed by two Officers that is delivered to the Trustee in accordance with the terms hereof. Each such certificate shall include the statements provided for in [Section 13.7](#), if and to the extent required by the provisions thereof.

“Opinion of Counsel” means an opinion in writing of legal counsel, who may be an employee of or counsel for the Company, that is delivered to the Trustee in accordance with the terms hereof. Each such opinion shall include the statements provided for in [Section 13.7](#), if and to the extent required by the provisions thereof.

“Original Issue Discount Security” means any Security which (i) is issued at a price lower than the amount payable upon the maturity thereof and (ii) provides for an amount less than the principal amount thereof to be due and payable upon redemption or a declaration of acceleration of the maturity thereof pursuant to [Section 6.1](#).

“Outstanding”, when used with reference to Securities of any series, means, subject to the provisions of [Section 8.4](#), as of any particular time, all Securities of that series theretofore authenticated and delivered by the Trustee under this Indenture, except (a) Securities theretofore canceled by the Trustee or any paying agent, or delivered to the Trustee or any paying agent for cancellation or that have previously been canceled; (b) Securities or portions thereof for the payment or redemption of which moneys or Governmental Obligations in the necessary amount shall have been deposited in trust with the Trustee or with any paying agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own paying agent); provided, however, that if such Securities or portions of such Securities are to be redeemed prior to the maturity thereof, notice of such redemption shall have been given as provided in Article Three, or provision satisfactory to the Trustee shall have been made for giving such notice; and (c) Securities in lieu of or in substitution for which other Securities shall have been authenticated and delivered pursuant to the terms of [Section 2.7](#).

“Person” means any individual, corporation, limited liability company, partnership, joint-venture, joint-stock company, unincorporated organization or government or any agency or political subdivision thereof.

“Predecessor Security” of any particular Security means every previous Security evidencing all or a portion of the same debt as that evidenced by such particular Security; and, for the purposes of this definition, any Security authenticated and delivered under [Section 2.7](#) in lieu of a lost, destroyed or stolen Security shall be deemed to evidence the same debt as the lost, destroyed or stolen Security.

“Regular Record Date” has the meaning set forth in [Section 2.3](#) hereof.

“Responsible Officer” when used with respect to the Trustee means any authorized officer within the Corporate Trust Department (or corresponding department bearing a different name) of the Trustee, including the president, any vice president, assistant vice president, assistant secretary, assistant treasurer, trust officer or any other officer of the Trustee who customarily performs functions similar to those performed by the Person who at the time shall be such officers, respectively, or to whom any corporate trust matter is referred because of his or her knowledge of and familiarity with the particular subject.

“Securities” means the debt Securities authenticated and delivered under this Indenture.

“Securities Act” means the Securities Act of 1933, as amended, as in effect at the date of execution of this instrument.

“Security Register” has the meaning set forth in Section 2.5(b) hereof.

“Security Registrar” has the meaning set forth in Section 2.5(b) hereof.

“Securityholder”, **“holder of Securities”**, **“registered holder”**, or other similar term, means the Person or Persons in whose name or names a particular Security shall be registered on the books of the Company kept for that purpose in accordance with the terms of this Indenture.

“Special Record Date” has the meaning set forth in Section 2.3 hereof.

“Subsidiary” means, in respect of any Person, any corporation, association, partnership, limited liability company, or other business entity of which more than 50% of the total voting power of shares of capital stock or other interests (including partnership interests) entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers or trustees thereof is at the time owned or controlled, directly or indirectly, by (a) such Person, (b) such Person and one or more Subsidiaries of such Person or (c) one or more Subsidiaries of such Person.

“Subsidiary Guarantor” means any Subsidiary of the Company that provides a Guarantee of the obligations of the Company with respect to any series of Securities or enters into a Guaranty Agreement that becomes a Subsidiary Guarantor.

“Subsidiary Guarantee” means a Guarantee, including any Guaranty Agreement, provided by a Subsidiary Guarantor of the Company’s obligations with respect to any series of Securities.

“Trustee” means _____, and, subject to the provisions of Article Seven, shall also include its successors and assigns, and, if at any time there is more than one Person acting in such capacity hereunder, “Trustee” shall mean each such Person. The term “Trustee” as used with respect to a particular series of the Securities shall mean the trustee with respect to that series.

“Trust Indenture Act” means the Trust Indenture Act of 1939, as amended, as in effect at the date of execution of this instrument, subject to the provisions of Sections 9.1, 9.2 and 10.1.

“Yield to Maturity” means the yield to maturity on a series of Securities, calculated at the time of issuance of such series, or, if applicable, at the most recent redetermination of interest on such series, and calculated in accordance with accepted financial practice.

ARTICLE II
ISSUE, DESCRIPTION, TERMS, EXECUTION, REGISTRATION AND EXCHANGE OF SECURITIES

Section 2.1 Designation and Terms of Securities.

(a) The aggregate principal amount of Securities that may be authenticated and delivered under this Indenture is unlimited. The Securities may be issued in one or more series up to the aggregate principal amount of Securities of that series from time to time authorized by or pursuant to a Board Resolution or pursuant to one or more indentures supplemental hereto. Prior to the initial issuance of Securities of any series, there shall be established in or pursuant to a Board Resolution, and set forth in an Officers’ Certificate, or established in one or more indentures supplemental hereto:

- (1) the title of the Security of the series (which shall distinguish the Securities of the series from all other Securities);
- (2) any limit upon the aggregate principal amount of the Securities of that series that may be authenticated and delivered under this Indenture (except for Securities authenticated and delivered upon registration of transfer of, or in exchange for, or in lieu of, other Securities of that series);
- (3) whether any of the Securities of the series will be issuable in whole or in part in temporary or permanent global form or in the form of book-entry securities and, in such case, the identity of the Depositary for such series;
- (4) the date or dates on which the principal of the Securities of the series is payable;
- (5) the rate or rates, which may be fixed or variable, at which the Securities of the series shall bear interest or the manner of calculation of such rate or rates, if any;
- (6) the date or dates from which such interest shall accrue, the Interest Payment Dates on which such interest will be payable or the manner of determination of such Interest Payment Dates and the record date for the determination of holders to whom interest is payable on any such Interest Payment Dates or the manner of determination of such record dates;
- (7) the place or places where payments with respect to the Securities of the series shall be payable;
- (8) the right, if any, to defer or extend payment of interest on the debt securities and the maximum length of any deferral or extension period;

- (9) the dates, if any, on which, the price or prices at which and the terms and conditions upon which, Securities of the series may be redeemed, in whole or in part, at the option of the Company;
- (10) the obligation, if any, of the Company to redeem or purchase Securities of the series pursuant to any sinking fund or analogous provisions (including payments made in cash in satisfaction of future sinking fund obligations) or at the option of a holder thereof and the date or dates, if any, on which, the price or prices at which, and the terms and conditions upon which, Securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- (11) if other than denominations of one thousand U.S. dollars (\$1,000) or any integral multiple thereof, the denominations in which the Securities of the series shall be issuable;
- (12) whether the series of Securities will be subject to any mandatory or optional sinking fund or similar provisions;
- (13) the currency or currency units in which payment of the principal of and any premium and interest on the Securities of the series shall be payable;
- (14) whether and under what circumstances the Company will pay additional amounts on the Securities of the series held by non-U.S. persons in respect of any tax, assessment or governmental charge withheld or deducted and, if so, whether the Company will have the option to redeem such Securities rather than pay such additional amounts;
- (15) the terms pursuant to which the Securities of the series are subject to defeasance and satisfaction and discharge;
- (16) any addition to, or modification or deletion of, any Events of Default or covenants provided for with respect to the Securities of the series;
- (17) the terms and conditions, if any, pursuant to which the Securities of the series are secured;
- (18) whether the Securities of the series will be convertible into shares of common stock or any other securities of the Company and, if so, the terms and conditions upon which such Securities will be so convertible, including whether conversion is mandatory, at the option of the holder, or at the option of the Company, the conversion price, the conversion period and any provisions pursuant to which the number of shares of common stock or other securities of the Company to be received by the holders of such series of Securities would be subject to adjustment;
- (19) if other than the principal amount thereof, the portion of the principal amount of Securities of the series which shall be payable upon declaration of acceleration of the maturity thereof pursuant to Section 6.1;

- (20) any provisions granting special rights to holders when a specified event occurs;
- if offered;
- (21) any special tax implications of the Securities of the series, including provisions for Original Issue Discount Securities;
- (22) the form of the Securities of the series, including the form of the Certificate of Authentication for such series; and
- (23) any and all other terms with respect to such series, including any terms which may be required by or advisable under United States laws or regulations or advisable in connection with the marketing of Securities of that series.

All Securities of any one series shall be substantially identical except as to denomination and except as may otherwise be provided in or pursuant to any such Board Resolution or in any indentures supplemental hereto.

If any of the terms of the series are established by action taken pursuant to a Board Resolution, a copy of an appropriate record of such action shall be certified by the Secretary or an Assistant Secretary of the Company and delivered to the Trustee at or prior to the delivery of the Officers' Certificate setting forth the terms of the series.

Securities of any particular series may be issued at various times, with different dates on which the principal or any installment of principal is payable, with different rates of interest, if any, or different methods by which rates of interest may be determined, with different dates on which such interest may be payable and with different redemption dates. Unless otherwise provided, a series may be reopened for issuances of additional Securities of such series.

Section 2.2 Form of Securities and Trustee's Certificate.

The Securities of any series and the Trustee's certificate of authentication to be borne by such Securities shall be substantially of the tenor and purport as set forth in one or more indentures supplemental hereto or as provided in a Board Resolution of the Company and as set forth in an Officers' Certificate of the Company and may have such letters, numbers or other marks of identification or designation and such legends or endorsements printed, lithographed or engraved thereon as the Company may deem appropriate and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any stock exchange on which Securities of that series may be listed, or to conform to usage.

Section 2.3 Denominations; Provisions for Payment.

The Securities shall be issuable as registered Securities and in the minimum denominations of one thousand U.S. dollars (\$1,000) or any integral multiple thereof, subject to Section 2.1(a)(11). The Securities of a particular series shall bear interest payable on the Interest Payment Dates and at the rate specified with respect to that series. Unless otherwise provided pursuant to Section 2.1, the principal of and the interest on the Securities of any series, as well as any premium thereon in case of redemption thereof prior to maturity, shall be payable in the coin or currency of the United States of America that at the time is legal tender for public and private debt, at the office or agency of the Company maintained for that purpose in the United States, unless otherwise specified with respect to any series of Securities, by the Corporate Trust Office of the Trustee. Each Security shall be dated the date of its authentication. Unless otherwise provided pursuant to Section 2.1, interest on the Securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

The interest installment on any Security that is payable, and is punctually paid or duly provided for, on any Interest Payment Date for Securities of that series shall be paid to the Person in whose name said Security (or one or more Predecessor Securities) is registered at the close of business on the applicable Business Day that is the Regular Record Date for such interest installment. Unless otherwise provided in the terms of a series of Securities, at the option of the Company, payment of interest may be mailed by check to the holders of the Securities of any series at their respective addresses set forth in the Security Register (as herein defined) or wired if held in book-entry form at The Depository Trust Company. In the event that any Security of a particular series or portion thereof is called for redemption and the redemption date is subsequent to a Regular Record Date with respect to any Interest Payment Date and on or prior to such Interest Payment Date, interest on such Security will be paid upon presentation and surrender of such Security as provided in Section 3.3.

Any interest on any Security that is payable, but is not punctually paid or duly provided for, on any Interest Payment Date for Securities of the same series (herein called "Defaulted Interest") shall forthwith cease to be payable to the registered holder on the relevant Regular Record Date by virtue of having been such holder; and such Defaulted Interest shall be paid by the Company, at its election, as provided in clause (1) or clause (2) below:

(1) The Company may make payment of any Defaulted Interest on Securities to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered at the close of business on the applicable Business Day that is a Special Record Date for the payment of such Defaulted Interest, which shall be fixed in the following manner: the Company shall notify the Trustee in writing of the amount of Defaulted Interest proposed to be paid on each such Security and the date of the proposed payment, and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount proposed to be paid in respect of such Defaulted Interest or shall make arrangements satisfactory to the Trustee for such deposit prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Interest as in this clause provided. The Trustee shall then fix a Special Record Date for the payment of such Defaulted Interest which shall not be more than 15 nor less than 10 days prior to the date of the proposed payment. The Trustee shall promptly notify the Company of such Special Record Date and, in the name and at the expense of the Company, shall cause notice of the proposed payment of such Defaulted Interest and the Special Record Date therefor to be mailed, first class postage prepaid, to each Securityholder at his or her address as it appears in the Security Register, not less than 10 days prior to such Special Record Date. Notice of the proposed payment of such Defaulted Interest and the Special Record Date therefor having been mailed as aforesaid, such Defaulted Interest shall be paid to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered on such Special Record Date and shall be no longer payable pursuant to the following clause (2).

(2) The Company may make payment of any Defaulted Interest on any Securities in any other lawful manner not inconsistent with the requirements of any securities exchange on which such Securities may be listed, and upon such notice as may be required by such exchange, if, after notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

Unless otherwise set forth in a Board Resolution or one or more indentures supplemental hereto establishing the terms of any series of Securities pursuant to Section 2.1 hereof, the term “Regular Record Date”, as used in this Section 2.3, with respect to a series of Securities with respect to any Interest Payment Date for such series shall mean either (i) the fifteenth day of the month immediately preceding the month in which an Interest Payment Date established for such series pursuant to Section 2.1 hereof shall occur, if such Interest Payment Date is the first day of a month, or (ii) the last day of the month immediately preceding the month in which an Interest Payment Date established for such series pursuant to Section 2.1 hereof shall occur, if such Interest Payment Date is the fifteenth day of a month, whether or not such date is a Business Day.

Subject to the foregoing provisions of this Section 2.3, each Security of a series delivered under this Indenture upon transfer of or in exchange for or in lieu of any other Security of such series shall carry the rights to interest accrued and unpaid, and to accrue, that were carried by such other Security.

Section 2.4 Execution and Authentication.

Two Officers shall sign the Securities for the Company by manual or facsimile signature. If an Officer whose signature is on a Security no longer holds that office at the time the Trustee authenticates the Security, the Security shall be valid nevertheless.

A Security shall not be valid until an authorized signatory of the Trustee or an Authentication Agent manually signs the certificate of authentication on the Security. The signature shall be conclusive evidence that the Security has been authenticated under this Indenture.

At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Securities of any series executed by the Company to the Trustee for authentication, together with a written order of the Company for the authentication and delivery of such Securities, signed by two Officers, and the Trustee shall authenticate and deliver such Securities in accordance with such written order.

In authenticating such Securities and accepting the additional responsibilities under this Indenture in relation to such Securities, the Trustee shall be entitled to receive, and (subject to Section 7.1) shall be fully protected in relying upon, an Opinion of Counsel and an Officers’ Certificate stating that the form and terms thereof have been established in conformity with the provisions of this Indenture.

The Trustee shall not be required to authenticate such Securities if the issue of such Securities pursuant to this Indenture will affect the Trustee's own rights, duties or immunities under the Securities and this Indenture or otherwise in a manner that is not reasonably acceptable to the Trustee.

Section 2.5 Registration of Transfer and Exchange.

(a) Securities of any series may be exchanged upon presentation thereof at the office or agency of the Company designated for such purpose in the United States, or such other location designated by the Company, for other Securities of such series of authorized denominations, and for a like aggregate principal amount, upon payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, all as provided in this Section 2.5. In respect of any Securities so surrendered for exchange, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in exchange therefor the Security or Securities of the same series that the Securityholder making the exchange shall be entitled to receive, bearing numbers not contemporaneously outstanding.

(b) The Company shall keep, or cause to be kept, at its office or agency designated for such purpose in the United States, or such other location designated by the Company a register or registers (herein referred to as the "Security Register") in which, subject to such reasonable regulations as it may prescribe, the Company shall register the Securities and the transfers of Securities as provided in this Article and which at all reasonable times shall be open for inspection by the Trustee. Unless otherwise specified in a supplemental indenture, the Trustee is hereby appointed as "Security Registrar" for the purpose of registering the Securities and the transfer of Securities of each series.

Upon surrender for transfer of any Security at the office or agency of the Company designated for such purpose, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in the name of the transferee or transferees a new Security or Securities of the same series as the Security presented for a like aggregate principal amount.

All Securities presented or surrendered for exchange or registration of transfer, as provided in this Section 2.5, shall be accompanied (if so required by the Company or the Security Registrar) by a written instrument or instruments of transfer, in form satisfactory to the Company or the Security Registrar, duly executed by the registered holder or by such holder's duly authorized attorney in writing.

(c) No service charge shall be made for any exchange or registration of transfer of Securities, or issue of new Securities in case of partial redemption of any series, but the Company may require payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, other than exchanges pursuant to Section 2.6, Section 3.3(b) and Section 9.4 not involving any transfer.

(d) The Company shall not be required (i) to issue, exchange or register the transfer of any Securities during a period beginning at the opening of business 15 days before the day of the mailing of a notice of redemption of less than all the Outstanding Securities of the same series and ending at the close of business on the day of such mailing, nor (ii) to register the transfer of or exchange any Securities of any series or portions thereof called for redemption except the unredeemed portion of any Securities of any series being redeemed in part. The provisions of this Section 2.5 are, with respect to any Global Security, subject to Section 2.11 hereof.

Section 2.6 Temporary Securities.

Pending the preparation of definitive Securities of any series, the Company may execute, and the Trustee shall authenticate and deliver, temporary Securities (printed, lithographed or typewritten) of any authorized denomination. Such temporary Securities shall be substantially in the form of the definitive Securities in lieu of which they are issued, but with such omissions, insertions and variations as may be appropriate for temporary Securities, all as may be determined by the Company. Every temporary Security of any series shall be executed by the Company and be authenticated by the Trustee upon the same conditions and in substantially the same manner, and with like effect, as the definitive Securities of such series. Without unnecessary delay, the Company will execute and will furnish definitive Securities of such series, and thereupon any or all temporary Securities of such series may be surrendered in exchange therefor (without charge to the holders), at the office or agency of the Company designated for the purpose, and the Trustee shall authenticate and such office or agency shall deliver in exchange for such temporary Securities an equal aggregate principal amount of definitive Securities of such series, unless the Company advises the Trustee to the effect that definitive Securities need not be executed and furnished until further notice from the Company. Until so exchanged, the temporary Securities of such series shall be entitled to the same benefits under this Indenture as definitive Securities of such series authenticated and delivered hereunder.

Section 2.7 Mutilated, Destroyed, Lost or Stolen Securities.

In case any temporary or definitive Security shall become mutilated or be destroyed, lost or stolen, the Company (subject to the next succeeding sentence) shall execute, and upon the Company's request the Trustee (subject as aforesaid) shall authenticate and deliver, a new Security of the same series, bearing a number not contemporaneously outstanding, in exchange and substitution for the mutilated Security, or in lieu of and in substitution for the Security so destroyed, lost or stolen. In every case the applicant for a substituted Security shall furnish to the Company and the Trustee such security or indemnity as may be required by them to save each of them harmless, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company and the Trustee evidence to their satisfaction of the destruction, loss or theft of the applicant's Security and of the ownership thereof. The Trustee may authenticate any such substituted Security and deliver the same upon the written request or authorization of any Officer of the Company. Upon the issuance of any substituted Security, the Company may require the payment of a sum sufficient to cover any tax or other governmental charge that may be imposed in relation thereto and any other expenses (including the fees and expenses of the Trustee) connected therewith. In case any Security that has matured or is about to mature shall become mutilated or be destroyed, lost or stolen, the Company may, instead of issuing a substitute Security, pay or authorize the payment of the same (without surrender thereof, except in the case of a mutilated Security) if the applicant for such payment shall furnish to the Company and the Trustee such security or indemnity as they may require to save each of them harmless, and, in case of destruction, loss or theft, evidence to the satisfaction of the Company and the Trustee of the destruction, loss or theft of such Security and of the ownership thereof.

Every replacement Security issued pursuant to the provisions of this Section 2.7 shall constitute an additional contractual obligation of the Company, whether or not the mutilated, destroyed, lost or stolen Security shall be found at any time, or be enforceable by anyone, and shall be entitled to all the benefits of this Indenture equally and proportionately with any and all other Securities of the same series duly issued hereunder. All Securities shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the replacement or payment of mutilated, destroyed, lost or stolen Securities, and shall preclude (to the extent lawful) any and all other rights or remedies, notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement or payment of negotiable instruments or other securities without their surrender.

Section 2.8 Cancellation.

All Securities surrendered for the purpose of payment, redemption, exchange or registration of transfer shall, if surrendered to the Company or any paying agent, be delivered to the Trustee for cancellation, or, if surrendered to the Trustee, shall be cancelled by it, and no Securities shall be issued in lieu thereof except as expressly required or permitted by any of the provisions of this Indenture. On request of the Company at the time of such surrender, the Trustee shall deliver to the Company any canceled Securities held by the Trustee. In the absence of such request, the Trustee may dispose of canceled Securities in accordance with its standard procedures and deliver a certificate of disposition to the Company. If the Company shall otherwise acquire any of the Securities, however, such acquisition shall not operate as a redemption or satisfaction of the indebtedness represented by such Securities unless and until the same are delivered to the Trustee for cancellation.

Section 2.9 Benefits of Indenture.

Nothing in this Indenture or in the Securities, express or implied, shall give or be construed to give to any Person, other than the parties hereto and the holders of the Securities, any legal or equitable right, remedy or claim under or in respect of this Indenture, or under any covenant, condition or provision herein contained, all such covenants, conditions and provisions being for the sole benefit of the parties hereto and of the holders of the Securities.

Section 2.10 Authenticating Agent.

So long as any of the Securities of any series remain Outstanding there may be an Authenticating Agent for any or all such series of Securities which the Trustee, with the written consent of the Company, shall have the right to appoint. Said Authenticating Agent shall be authorized to act on behalf of the Trustee to authenticate Securities of such series issued upon exchange, transfer or partial redemption thereof, and Securities so authenticated shall be entitled to the benefits of this Indenture and shall be valid and obligatory for all purposes as if authenticated by the Trustee hereunder. All references in this Indenture to the authentication of Securities by the Trustee shall be deemed to include authentication by an Authenticating Agent for such series. Each Authenticating Agent shall be a corporation that has a combined capital and surplus, as most recently reported or determined by it, sufficient under the laws of any jurisdiction under which it is organized or in which it is doing business to conduct a trust business, and that is otherwise authorized under such laws to conduct such business and is subject to supervision or examination by Federal or State authorities. If at any time any Authenticating Agent shall cease to be eligible in accordance with these provisions, it shall resign immediately.

Any Authenticating Agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time (and upon request by the Company shall) terminate the agency of any Authenticating Agent by giving written notice of termination to such Authenticating Agent and to the Company. Upon resignation, termination or cessation of eligibility of any Authenticating Agent, the Trustee may appoint an eligible successor Authenticating Agent acceptable to the Company. Any successor Authenticating Agent, upon acceptance of its appointment hereunder, shall become vested with all the rights, powers and duties of its predecessor hereunder as if originally named as an Authenticating Agent pursuant hereto.

Section 2.11 Global Securities.

(a) If the Company shall establish pursuant to Section 2.1 that the Securities of a particular series are issuable as a Global Security, then the Company shall execute and the Trustee shall, in accordance with Section 2.4, authenticate and deliver, a Global Security that (i) shall represent, and shall be denominated in an amount equal to the aggregate principal amount of, such of the Outstanding Securities of such series as shall be specified therein and that the aggregate amount of Outstanding Securities represented thereby may from time to time be increased or reduced to reflect exchanges, (ii) shall be registered in the name of the Depository or its nominee, (iii) shall be delivered by the Trustee to the Depository or pursuant to the Depository's instruction and (iv) shall bear a legend substantially to the following effect: "Except as otherwise provided in Section 2.11 of the Indenture, this Security may be transferred, in whole but not in part, only to another nominee of the Depository or to a successor Depository or to a nominee of such successor Depository." Any endorsement of a Security in global form to reflect the amount, or any increase or decrease in the amount, of Outstanding Securities represented thereby shall be made by the Trustee in such manner and upon instructions given by such Person or Persons as shall be specified therein or in the written request signed in the name of the Company, by two Officers thereof to be delivered to the Trustee pursuant to Section 2.4 or Section 2.6.

(b) Notwithstanding the provisions of Section 2.5, the Global Security of a series may be transferred, in whole but not in part, and in the manner provided in Section 2.5, only to another nominee of the Depository for such series, or to a successor Depository for such series selected or approved by the Company or to a nominee of such successor Depository.

(c) If at any time the Depositary for a series of the Securities notifies the Company that it is unwilling or unable to continue as Depositary for such series or if at any time the Depositary for such series shall no longer be registered or in good standing under the Exchange Act, or other applicable statute or regulation, and a successor Depositary for such series is not appointed by the Company within 90 days after the Company receives such notice or becomes aware of such condition, as the case may be, this Section 2.11 shall no longer be applicable to the Securities of such series and the Company will execute, and subject to Section 2.5, the Trustee will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. In addition, the Company may at any time determine that the Securities of any series shall no longer be represented by a Global Security and that the provisions of this Section 2.11 shall no longer apply to the Securities of such series. In such event the Company will execute and subject to Section 2.5, the Trustee, upon receipt of an Officers' Certificate evidencing such determination by the Company, will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. Upon the exchange of the Global Security for such Securities in definitive registered form without coupons, in authorized denominations, the Global Security shall be canceled by the Trustee. Such Securities in definitive registered form issued in exchange for the Global Security pursuant to this Section 2.11(c) shall be registered in such names and in such authorized denominations as the Depositary, pursuant to instructions from its direct or indirect participants or otherwise, shall instruct the Trustee. The Trustee shall deliver such Securities to the Depositary for delivery to the Persons in whose names such Securities are so registered.

(d) If an Event of Default has occurred and is continuing with respect to a particular series of the Securities, the Company may execute, and the Trustee, upon receipt of an Officers' Certificate directing the authorization and delivery thereof, shall authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security.

Section 2.12 No Obligation of the Trustee.

(a) The Trustee shall have no responsibility or obligation to any beneficial owner of a Global Security, a member of, or a participant in, the Depositary or other Person with respect to the accuracy of the records of the Depositary or its nominee or of any participant or member thereof, with respect to any ownership interest in the Securities or with respect to the delivery to any participant, member, beneficial owner or other Person (other than the Depositary) of any notice (including any notice of redemption) or the payment of any amount or delivery of any Securities (or other security or property) under or with respect to such Securities. All notices and communications to be given to the Holders and all payments to be made to Holders in respect of the Securities shall be given or made only to or upon the order of the registered Holder or Holders (which shall be the Depositary or its nominee in the case of a Global Security). The rights of beneficial owners in any Global Security shall be exercised only through the Depositary, subject to the applicable rules and procedures of the Depositary. The Trustee may rely and shall be fully protected in relying upon information furnished by the Depositary with respect to its members, participants and any beneficial owners.

(b) The Trustee shall have no obligations or duty to monitor, determine or inquire as to compliance with any restrictions on transfer imposed under this Indenture or under applicable law with respect to any transfer of any interest in any Security (including any transfers between or among the Depository participants, members or beneficial owners in any Global Security) other than to require delivery of such certificates and other documentation or evidence as are expressly required by, and to do so if and when expressly required by, the terms of this Indenture, and to examine the same to determine substantial compliance as to form with the express requirements hereof.

ARTICLE III REDEMPTION OF SECURITIES AND SINKING FUND PROVISIONS

Section 3.1 Redemption.

The Company may redeem the Securities of any series issued hereunder on and after the dates and in accordance with the terms established for such series pursuant to Section 2.1 hereof.

Section 3.2 Notice of Redemption.

(a) In case the Company shall desire to exercise such right to redeem all or, as the case may be, a portion of the Securities of any series in accordance with the right reserved in such Securities so to do, the Company shall, or shall cause the Trustee to, give notice of such redemption to holders of the Securities of such series to be redeemed by sending electronically or by mailing, first class postage prepaid, a notice of such redemption not less than 30 days and not more than 60 days before the date fixed for redemption of that series to such holders at their last addresses as they shall appear upon the Security Register, unless a shorter period is specified in the Securities to be redeemed. Any notice that is sent in the manner herein provided shall be conclusively presumed to have been duly given, whether or not the registered holder receives the notice. In any case, failure to duly give such notice to the holder of any Security of any series designated for redemption in whole or in part, or any defect in the notice, shall not affect the validity of the proceedings for the redemption of any other Securities of such series or any other series. In the case of any redemption of Securities prior to the expiration of any restriction on such redemption provided in the terms of such Securities or elsewhere in this Indenture, the Company shall furnish the Trustee with an Officers' Certificate evidencing compliance with any such restriction.

Each such notice of redemption shall specify the date fixed for redemption and the redemption price (or the manner of calculation thereof) at which Securities of that series are to be redeemed, and shall state that payment of the redemption price of such Securities to be redeemed will be made at the office or agency of the Company in the United States, upon presentation and surrender of such Securities, that interest accrued to the date fixed for redemption will be paid as specified in said notice, that from and after said date interest will cease to accrue and that the redemption is for a sinking fund, if such is the case. If less than all the Securities of a series are to be redeemed, the notice to the holders of Securities of that series to be redeemed in whole or in part shall specify the particular Securities to be so redeemed. In case any Security is to be redeemed in part only, the notice that relates to such Security shall state the portion of the principal amount thereof to be redeemed, and shall state that on and after the redemption date, upon surrender of such Security, a new Security or Securities of such series in principal amount equal to the unredeemed portion thereof will be issued.

(b) If less than all the Securities of a series are to be redeemed, the Company shall give the Trustee at least 30 days' notice in advance of the date fixed for redemption as to the aggregate principal amount of Securities of the series to be redeemed, and thereupon the Trustee shall select, by lot on a pro rata basis or in such other manner as it shall deem appropriate and fair in its discretion. The portion of the principal amount of Securities so selected for partial redemption shall be equal to the minimum authorized denomination for Securities of that series or any integral multiple thereof. Upon making its selection, the Trustee shall promptly notify the Company in writing of the numbers of the Securities to be redeemed, in whole or in part.

Unless otherwise provided in the applicable supplemental indenture, the Company shall not be required to issue, register the transfer of, or exchange any Securities of a series that are subject to redemption during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of less than all of that series of Securities that may be selected for redemption and ending at the close of business on the day of such mailing.

The Company may, if and whenever it shall so elect, by delivery of instructions signed on its behalf by any Officer, instruct the Trustee or any paying agent to call all or any part of the Securities of a particular series for redemption and to give notice of redemption in the manner set forth in this Section 3.2, such notice to be in the name of the Company or its own name, as the Trustee or such paying agent may deem advisable. In any case in which notice of redemption is to be given by the Trustee or any such paying agent, the Company shall deliver or cause to be delivered to, or permit to remain with, the Trustee or such paying agent, as the case may be, such Security Register, transfer books or other records, or suitable copies or extracts therefrom, sufficient to enable the Trustee or such paying agent to give any notice by mail that may be required under this Section 3.2.

Section 3.3 Payment Upon Redemption.

(a) If the giving of notice of redemption shall have been completed as above provided, the Securities or portions of Securities of the series to be redeemed specified in such notice shall become due and payable on the date and at the place stated in such notice at the applicable redemption price, together with interest accrued to the date fixed for redemption. Interest on such Securities or portions of Securities shall cease to accrue on and after the date fixed for redemption, unless the Company shall default in the payment of such redemption price and accrued interest with respect to any such Security or portion thereof. On presentation and surrender of such Securities on or after the date fixed for redemption at the place of payment specified in the notice, said Securities shall be paid and redeemed at the applicable redemption price for such series, together with interest accrued thereon to the date fixed for redemption. However, if the date fixed for redemption is subsequent to a Regular Record Date with respect to any Interest Payment Date and on or prior to such Interest Payment Date, the interest installment payable on such date shall be payable to the registered holder at the close of business on the applicable Regular Record Date pursuant to Section 2.3.

(b) Upon presentation of any Security of such series that is to be redeemed in part only, the Company shall execute and the Trustee shall authenticate and the office or agency where the Security is presented shall deliver to the holder thereof, at the expense of the Company, a new Security of the same series of authorized denominations in principal amount equal to the unredeemed portion of the Security so presented.

Section 3.4 Sinking Fund.

The provisions of Sections 3.4, 3.5 and 3.6 shall be applicable to any sinking fund for the retirement of Securities of a series, except as otherwise specified as contemplated by Section 2.1 for Securities of such series.

The minimum amount of any sinking fund payment provided for by the terms of Securities of any series is herein referred to as a “mandatory sinking fund payment”, and any payment in excess of such minimum amount provided for by the terms of Securities of any series is herein referred to as an “optional sinking fund payment”. If provided for by the terms of Securities of any series, the cash amount of any sinking fund payment may be subject to reduction as provided in Section 3.5. Each sinking fund payment shall be applied to the redemption of Securities of any series as provided for by the terms of Securities of such series.

Section 3.5 Satisfaction of Sinking Fund Payments with Securities.

The Company (i) may deliver Outstanding Securities of a series (other than any Securities previously called for redemption) and (ii) may apply as a credit Securities of a series that have been redeemed either at the election of the Company pursuant to the terms of such Securities or through the application of permitted optional sinking fund payments pursuant to the terms of such Securities, in each case in satisfaction of all or any part of any sinking fund payment with respect to the Securities of such series required to be made pursuant to the terms of such Securities as provided for by the terms of such series, provided that such Securities have not been previously so credited. Such Securities shall be received and credited for such purpose by the Trustee at the redemption price specified in such Securities for redemption through operation of the sinking fund and the amount of such sinking fund payment shall be reduced accordingly.

Section 3.6 Redemption of Securities for Sinking Fund.

Not less than 45 days prior to each sinking fund payment date for any series of Securities, the Company will deliver to the Trustee an Officers' Certificate specifying the amount of the next ensuing sinking fund payment for that series pursuant to the terms of the series, the portion thereof, if any, that is to be satisfied by delivering and crediting Securities of that series pursuant to Section 3.5 and the basis for such credit and will, together with such Officers' Certificate, deliver to the Trustee any Securities to be so delivered. Not less than 30 days before each such sinking fund payment date, the Trustee shall select the Securities to be redeemed upon such sinking fund payment date in the manner specified in Section 3.2 and cause notice of the redemption thereof to be given in the name of and at the expense of the Company in the manner provided in Section 3.2. Such notice having been duly given, the redemption of such Securities shall be made upon the terms and in the manner stated in Section 3.3.

**ARTICLE IV
CERTAIN COVENANTS**

Section 4.1 Payment of Principal, Premium and Interest.

The Company will duly and punctually pay or cause to be paid the principal of and any premium and interest on the Securities of that series at the time and place and in the manner provided herein and established with respect to such Securities.

Section 4.2 Maintenance of Office or Agency.

So long as any series of the Securities remain Outstanding, the Company agrees to maintain an office or agency in the United States with respect to each such series, where (i) Securities of that series may be presented for payment, (ii) Securities of that series may be presented as hereinabove authorized for registration of transfer and exchange and (iii) notices and demands to or upon the Company in respect of the Securities of that series and this Indenture may be given or served, such designation to continue with respect to such office or agency until the Company shall, by written notice signed by an Officer and delivered to the Trustee, designate some other office or agency for such purposes or any of them. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, notices and demands may be made or served at the Corporate Trust Office of the Trustee, and the Company hereby appoints the Trustee as its agent to receive all such presentations, notices and demands.

Section 4.3 Paying Agents.

(a) If the Company shall appoint one or more paying agents for all or any series of the Securities, other than the Trustee, the Company will cause each such paying agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section 4.3:

- (1) that it will hold all sums held by it as such agent for the payment of the principal of and any premium or interest on the Securities of that series (whether such sums have been paid to it by the Company or by any other obligor of such Securities) in trust for the benefit of the Persons entitled thereto;
- (2) that it will give the Trustee notice of any failure by the Company (or by any other obligor of such Securities) to make any payment of the principal of and any premium or interest on the Securities of that series when the same shall be due and payable;
- (3) that it will, at any time during the continuance of any failure referred to in the preceding paragraph (a)(2) above, upon the written request of the Trustee, forthwith pay to the Trustee all sums so held in trust by such paying agent; and
- (4) that it will perform all other duties of paying agent as set forth in this Indenture.

(b) If the Company shall act as its own paying agent with respect to any series of the Securities, it shall on or before each due date of the principal of and any premium or interest on Securities of that series, set aside, segregate and hold in trust for the benefit of the Persons entitled thereto, a sum sufficient to pay such principal and any premium or interest so becoming due on Securities of that series until such sums shall be paid to such Persons or otherwise disposed of as herein provided, and will promptly notify the Trustee of such action, or any failure (by it or any other obligor on such Securities) to take such action. Whenever the Company shall have one or more paying agents for any series of Securities, it will, prior to each due date of the principal of and any premium or interest on any Securities of that series, deposit with the paying agent a sum sufficient to pay the principal and any premium or interest so becoming due, such sum to be held in trust for the benefit of the Persons entitled to such principal, premium or interest, and (unless such paying agent is the Trustee) the Company shall promptly notify the Trustee of this action or failure so to act.

(c) Notwithstanding anything in this Section 4.3 to the contrary, (i) the agreement to hold sums in trust as provided in this Section is subject to the provisions of Section 11.5 and (ii) the Company may at any time, for the purpose of obtaining the satisfaction and discharge of this Indenture or for any other purpose, pay, or direct any paying agent to pay, to the Trustee all sums held in trust by the Company or such paying agent, such sums to be held by the Trustee upon the same terms and conditions as those upon which such sums were held by the Company or such paying agent; upon such payment by any paying agent to the Trustee, such paying agent shall be released from all further liability with respect to such money.

Section 4.4 Appointment to Fill Vacancy in Office of Trustee.

The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the manner provided in Section 7.10, a Trustee, so that there shall at all times be a Trustee hereunder.

Section 4.5 Compliance with Consolidation Provisions.

The Company will not, while any of the Securities remain Outstanding, consolidate with, or merge into, or merge into itself, or sell or convey all or substantially all of its property to any other company unless the provisions of Article Ten hereof are complied with.

Section 4.6 Statement by Officers as to Default.

The Company will deliver to the Trustee, within 120 days after the end of each fiscal year of the Company ending after the date hereof, an Officers' Certificate signed by its principal executive officer, principal financial officer or principal accounting officer stating whether or not to the best knowledge of the signer thereof, the Company is in default in the performance or observance of any of the terms, provisions and conditions of this Indenture, and if the Company shall be in default, specifying all such defaults and the nature and status thereof of which they may have knowledge.

ARTICLE V
SECURITYHOLDERS' LISTS AND REPORTS BY THE COMPANY AND THE TRUSTEE

Section 5.1 Company to Furnish Names and Addresses of Securityholders to Trustee.

The Company will furnish or cause to be furnished to the Trustee (a) semiannually on _____ and _____, a list, in such form as the Trustee may reasonably require, of the names and addresses of the holders of each series of Securities as of such date, provided that the Company shall not be obligated to furnish or cause to be furnished such list at any time that the list shall not differ in any respect from the most recent list furnished to the Trustee by the Company and (b) at such other times as the Trustee may request in writing within 30 days after the receipt by the Company of any such request, a list of similar form and content as of a date not more than 15 days prior to the time such list is furnished; provided, however, that, in either case, no such list need be furnished for any series of Securities for which the Trustee shall be the Security Registrar.

Section 5.2 Preservation of Information; Communications with Securityholders.

(a) The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the holders of Securities contained in the most recent list furnished to it as provided in Section 5.1 and as to the names and addresses of holders of Securities received by the Trustee in its capacity as Security Registrar (if acting in such capacity).

(b) The Trustee may destroy any list furnished to it as provided in Section 5.1 upon receipt of a new list so furnished.

(c) Securityholders may communicate as provided in Section 312(b) of the Trust Indenture Act with other Securityholders with respect to their rights under this Indenture or under the Securities. The Company, the Trustee, the Security Registrar and anyone else shall have the protection of Section 312(c) of the Trust Indenture Act with respect to the sending of any material pursuant to a request made pursuant to Section 312(b) of the Trust Indenture Act.

Section 5.3 Reports by the Company.

(a) The Company covenants and agrees to file with the Trustee (unless such reports have been filed on the Securities and Exchange Commission's Electronic Data Gathering, Analysis, and Retrieval system), within 15 days after the Company files the same with the Securities and Exchange Commission, copies of the annual reports and of the information, documents and other reports (or copies of such portions of any of the foregoing as the Securities and Exchange Commission may from time to time by rules and regulations prescribe) that the Company may be required to file with the Securities and Exchange Commission pursuant to Section 13 or Section 15(d) of the Exchange Act. If the Company is no longer required to file information, documents or reports pursuant to either of such sections of the Exchange Act, the Company shall continue to provide the Trustee with reports containing substantially the same information as would have been required to be filed with the Securities Exchange Commission had the Company continued to have been subject to such reporting requirements. In such event, such reports shall be provided to the Trustee within 15 days after the dates applicable to a registrant that is not an accelerated filer or a large accelerated filer on which the Company would have been required to provide reports to the Securities and Exchange Commission had it continued to have been subject to such reporting requirements. For the avoidance of doubt, the Company shall also comply with the other provisions of Section 314(a) of the Trust Indenture Act.

(b) The Company covenants and agrees to file with the Trustee and the Securities and Exchange Commission, in accordance with the rules and regulations prescribed from time to time by the Securities and Exchange Commission, such additional information, documents and reports with respect to compliance by the Company with the conditions and covenants provided for in this Indenture as may be required from time to time by such rules and regulations.

(c) The Company covenants and agrees to transmit electronically or by mail, first class postage prepaid, or reputable over-night delivery service that provides for evidence of receipt, to the Securityholders, as their names and addresses appear upon the Security Register, within 30 days after the filing thereof with the Trustee, such summaries of any information, documents and reports required to be filed by the Company pursuant to subsections (a) and (b) of this Section 5.3 as may be required by rules and regulations prescribed from time to time by the Securities and Exchange Commission.

Section 5.4 Reports by the Trustee.

(a) On or before _____ in each year in which any of the Securities are Outstanding, the Trustee shall transmit by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register, a brief report dated as of the preceding _____, if and to the extent required under Section 313(a) of the Trust Indenture Act, detailing certain events that occurred within the previous 12 months.

(b) The Trustee shall comply with Sections 313(b) and 313(c) of the Trust Indenture Act.

(c) A copy of each such report shall, at the time of such transmission to Securityholders, be filed by the Trustee with the Company, with each stock exchange upon which any Securities are listed (if so listed) and also with the Securities and Exchange Commission. The Company agrees to notify the Trustee when any Securities become listed on any stock exchange.

ARTICLE VI

REMEDIES OF THE TRUSTEE AND SECURITYHOLDERS ON EVENT OF DEFAULT

Section 6.1 Events of Default.

(a) Whenever used herein with respect to Securities of a particular series, "Event of Default" means any one or more of the following events that has occurred and is continuing:

(1) the Company defaults in the payment of any installment of interest upon any of the Securities of that series, as and when the same shall become due and payable, and continuance of such default for a period of 30 days; provided, however, that a valid extension of an interest payment period by the Company in accordance with the terms of any indenture supplemental hereto, shall not constitute a default in the payment of interest for this purpose;

(2) the Company defaults in the payment of the principal of (or premium, if any, on) any of the Securities of that series as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to that series; provided, however, that a valid extension of the maturity of such Securities in accordance with the terms of any indenture supplemental hereto, shall not constitute a default in the payment of principal or any premium for this purpose;

(3) the Company fails to observe or perform any other of its covenants or agreements with respect to that series contained in this Indenture or otherwise established with respect to that series of Securities pursuant to Section 2.1 hereof (other than a covenant or agreement that has been expressly included in this Indenture solely for the benefit of one or more series of Securities other than such series) for a period of 60 days after the date on which written notice of such failure, requiring the same to be remedied and stating that such notice is a "Notice of Default" hereunder, shall have been given in writing to the Company by the Trustee, or to the Company and the Trustee by the holders of at least 25% in principal amount of the Securities of that series at the time Outstanding;

(4) if the Securities of the series are convertible into shares of common stock or other securities of the Company, failure by the Company to deliver common stock or the other securities when the holder or holders of such Securities elect to convert such Securities into shares of common stock or other securities of the Company;

(5) the Company pursuant to or within the meaning of any Bankruptcy Law (i) commences a voluntary case, (ii) consents to the entry of an order for relief against it in an involuntary case, (iii) consents to the appointment of a Custodian of it or for all or substantially all of its property or (iv) makes a general assignment for the benefit of its creditors;

(6) a court of competent jurisdiction enters an order under any Bankruptcy Law that (i) is for relief against the Company in an involuntary case, (ii) appoints a Custodian of the Company for all or substantially all of its property or (iii) orders the liquidation of the Company, and, in each such case, the order or decree remains unstayed and in effect for 90 days; or

(7) any other Event of Default provided with respect to Securities of that series.

(b) In each and every such case (other than an Event of Default specified in clauses (5) or (6) above), unless the principal of all the Securities of that series shall have already become due and payable, either the Trustee or the holders of not less than 25% in aggregate principal amount of the Securities of that series then Outstanding hereunder, by notice in writing to the Company (and to the Trustee, if given by such Securityholders), may declare the principal (or, if the Securities of such series are Original Issue Discount Securities, such portion of the principal amount as may be specified in the terms of such series) of, premium, if any, and accrued interest, if any, on all the Securities of that series to be due and payable immediately, and upon any such declaration the same shall become and shall be immediately due and payable, notwithstanding anything contained in this Indenture or in the Securities of that series or established with respect to that series pursuant to Section 2.1 to the contrary. If an Event of Default specified in clauses (5) or (6) above occurs, all unpaid principal (or, if the Securities of such series are Original Issue Discount Securities, such portion of the principal amount as may be specified in the terms of such series) of, premium, if any, and accrued interest, if any, on, all the Securities of that series then outstanding will become automatically due and payable immediately, without any declaration or other act on the part of the Trustee or any holder.

(c) At any time after the principal of the Securities of that series shall have been so declared due and payable, and before any judgment or decree for the payment of the moneys due shall have been obtained or entered as hereinafter provided, the holders of a majority in aggregate principal amount of the Securities of that series then Outstanding hereunder, by written notice to the Company and the Trustee, may rescind and annul such declaration and its consequences if: (i) the Company has paid or deposited with the Trustee a sum sufficient to pay all matured installments of interest upon all the Securities of that series and the principal of (and premium, if any, on) any and all Securities of that series that shall have become due otherwise than by acceleration (with interest upon such principal and premium, if any, and, to the extent that such payment is enforceable under applicable law, upon overdue installments of interest, at the rate per annum or Yield to Maturity (in the case of Original Issue Discount Securities) expressed in the Securities of that series (or at the respective rates of interest or Yields to Maturity of all the Securities, as the case may be) to the date of such payment or deposit) and any amount payable to the Trustee under Section 7.6, and (ii) any and all Events of Default under the Indenture with respect to such series, other than the non-payment of principal, premium, if any, or interest on Securities of that series that (or, if any Securities are Original Issue Discount Securities, such portion of the principal as may be specified in the terms thereof) shall not have become due by their terms, shall have been remedied or waived as provided in Section 6.6.

No such rescission and annulment shall extend to or shall affect any subsequent default or impair any right consequent thereon.

(d) In case the Trustee shall have proceeded to enforce any right with respect to Securities of that series under this Indenture and such proceedings shall have been discontinued or abandoned because of such rescission or annulment or for any other reason or shall have been determined adversely to the Trustee, then and in every such case, the Company and the Trustee shall be restored respectively to their former positions and rights hereunder, and all rights, remedies and powers of the Company and the Trustee shall continue as though no such proceedings had been taken.

Section 6.2 Collection of Indebtedness and Suits for Enforcement by Trustee.

(a) The Company covenants that (i) in case it shall default in the payment of any installment of interest on any of the Securities of a series, or any payment required by any sinking or analogous fund established with respect to that series as and when the same shall have become due and payable, and such default shall have continued for a period of 30 days, or (ii) in case it shall default in the payment of the principal of (or premium, if any, on) any of the Securities of a series when the same shall have become due and payable, whether upon maturity of the Securities of a series or upon redemption or upon declaration or otherwise, then, upon demand of the Trustee, the Company will pay to the Trustee, for the benefit of the holders of the Securities of that series, the whole amount that then shall have become due and payable on all such Securities for principal (and premium, if any) or interest, or both, as the case may be, with interest upon the overdue principal (and premium, if any) and (to the extent that payment of such interest is enforceable under applicable law) upon overdue installments of interest at the rate per annum expressed in the Securities of that series; and, in addition thereto, such further amount as shall be sufficient to cover the reasonable costs and expenses of collection, and the amount payable to the Trustee under Section 7.6.

(b) If the Company shall fail to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, shall be entitled and empowered to institute any action or proceedings at law or in equity for the collection of the sums so due and unpaid, and may prosecute any such action or proceeding to judgment or final decree, and may enforce any such judgment or final decree against the Company or other obligor upon the Securities of that series and collect the moneys adjudged or decreed to be payable in the manner provided by law out of the property of the Company or other obligor upon the Securities of that series, wherever situated.

(c) In case of any receivership, insolvency, liquidation, bankruptcy, reorganization, readjustment, arrangement, composition or judicial proceedings affecting the Company, or its creditors or property, the Trustee shall have power to intervene in such proceedings and take any action therein that may be permitted by the court and shall (except as may be otherwise provided by law) be entitled to file such proofs of claim and other papers and documents as may be necessary or advisable in order to have the claims of the Trustee and of the holders of Securities of such series allowed for the entire amount due and payable by the Company under this Indenture at the date of institution of such proceedings and for any additional amount that may become due and payable by the Company after such date, and to collect and receive any moneys or other property payable or deliverable on any such claim, and to distribute the same after the deduction of the amount payable to the Trustee under Section 7.6; any receiver, assignee or trustee in bankruptcy or reorganization is hereby authorized by each of the holders of Securities of such series to make such payments to the Trustee, and, in the event that the Trustee shall consent to the making of such payments directly to such Securityholders, to pay to the Trustee any amount due it under Section 7.6.

(d) All rights of action and of asserting claims under this Indenture, or under any of the terms established with respect to Securities of that series, may be enforced by the Trustee without the possession of any of such Securities, or the production thereof at any trial or other proceeding relating thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for payment to the Trustee of any amounts due under Section 7.6, be for the ratable benefit of the holders of the Securities of such series.

In case of an Event of Default hereunder, the Trustee may, in its discretion, proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as the Trustee shall deem most effective to protect and enforce any of such rights, either at law or in equity or in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in the Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law.

Nothing contained herein shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Securityholder any plan of reorganization, arrangement, adjustment or composition affecting the Securities of that series or the rights of any holder thereof or to authorize the Trustee to vote in respect of the claim of any Securityholder in any such proceeding.

Section 6.3 Application of Moneys Collected.

Any moneys collected by the Trustee pursuant to this Article with respect to a particular series of Securities shall be applied in the following order, at the date or dates fixed by the Trustee and, in case of the distribution of such moneys on account of principal (or premium, if any) or interest (upon presentation of the Securities of that series and notation thereon the payment if only partially paid) and upon surrender thereof (if fully paid):

FIRST: To the payment of costs and expenses of collection and of all amounts payable to the Trustee under Section 7.6; and

SECOND: To the payment of the amounts then due and unpaid upon the Securities of such series for principal and any premium and interest, in respect of which or for the benefit of which such money has been collected, ratably, without preference or priority of any kind, according to the amounts due and payable on such Securities for principal and any premium and interest, respectively.

Section 6.4 Limitation on Suits.

No holder of a Security of any series shall have any right by virtue or by availing of any provision of this Indenture to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture or for the appointment of a receiver or trustee, or for any other remedy hereunder, unless (i) such holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof with respect to the Securities of such series specifying such Event of Default, as hereinbefore provided; (ii) the holders of not less than 25% in aggregate principal amount of the Securities of such series then Outstanding shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as trustee hereunder; (iii) such holder or holders shall have offered to the Trustee such reasonable indemnity satisfactory to it against the costs, expenses and liabilities to be incurred therein or thereby; and (iv) the Trustee for 60 days after its receipt of such notice, request and offer of indemnity, shall have failed to institute any such action, suit or proceeding; and (v) during such 60 day period, the holders of a majority in principal amount of the Securities of that series do not give the Trustee a direction inconsistent with the request.

Notwithstanding anything contained herein to the contrary or any other provisions of this Indenture, the right of any holder of any Security to receive payment of the principal of and any premium and (subject to Section 2.3) interest on such Security (whether upon redemption, repurchase, maturity or otherwise) or payment or delivery of any amounts due upon conversion of Securities of any series that are convertible into shares of common stock or other securities, as therein provided, on or after the respective due dates expressed in such Security (or in the case of redemption or repurchase, on the redemption date or repurchase date, respectively), or to institute suit for the enforcement of any such payment or delivery on or after such respective dates (including the redemption date or repurchase date, as applicable) shall not be impaired or affected without the consent of such holder. By accepting a Security hereunder, it is expressly understood, intended and covenanted by the taker and holder of every Security of such series with every other such taker and holder and the Trustee, that no one or more holders of Securities of such series shall have any right in any manner whatsoever by virtue or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of the holders of any other of such Securities, or to obtain or seek to obtain priority over or preference to any other such holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all holders of Securities of such series. For the protection and enforcement of the provisions of this Section 6.4, each and every Securityholder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Section 6.5 Rights and Remedies Cumulative; Delay or Omission Not Waiver.

(a) Except as otherwise provided in Section 2.7, all powers and remedies given by this Article to the Trustee or to the Securityholders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any other powers and remedies available to the Trustee or the holders of the Securities, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture or otherwise established with respect to such Securities.

(b) No delay or omission of the Trustee or of any holder of any of the Securities to exercise any right or power accruing upon any Event of Default occurring and continuing as aforesaid shall impair any such right or power, or shall be construed to be a waiver of any such default or on acquiescence therein; and, subject to the provisions of Section 6.4, every power and remedy given by this Article or by law to the Trustee or the Securityholders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Securityholders.

Section 6.6 Control by Securityholders.

The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding, determined in accordance with Section 8.4, shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred on the Trustee with respect to such series; provided, however, that such direction shall not be in conflict with any rule of law or with this Indenture or be unduly prejudicial to the rights of holders of Securities of such series not consenting; and provided, further, that the Trustee may take any other action deemed proper by the Trustee which is not inconsistent with such direction. Prior to the taking of any action hereunder, the Trustee shall be entitled to reasonable indemnification satisfactory to the Trustee against all losses and expenses caused by taking or not taking such action. Subject to the provisions of Section 7.1, the Trustee shall have the right to decline to follow any such direction if the Trustee in good faith shall, by a Responsible Officer or Officers of the Trustee, determine that the proceeding so directed would involve the Trustee in personal liability. The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding affected thereby, determined in accordance with Section 8.4, may determine, and may have the Trustee on behalf of the holders of all of the Securities of such series waive any past default in the performance of any of the covenants contained herein or established pursuant to Section 2.1 with respect to such series and its consequences, except for (a) a default in the payment of the principal of or any premium or interest on, any of the Securities of that series (whether upon redemption, repurchase, maturity or otherwise) or payment or delivery of any amounts due upon conversion of Securities of any series that are convertible into shares of common stock or other securities as and when the same shall become due by the terms of such Securities otherwise than by acceleration (unless such default has been cured and a sum sufficient to pay all matured installments of interest and principal and any premium has been deposited with the Trustee (in accordance with Section 6.1(c)), or (b) if the Securities of that series are convertible into shares of common stock or other securities, the failure by the Company to deliver common stock or the other securities, as and when they shall become deliverable by the terms of such Securities. Upon any such waiver, the default covered thereby shall be deemed to be cured for all purposes of this Indenture and the Company, the Trustee and the holders of the Securities of such series shall be restored to their former positions and rights hereunder, respectively; but no such waiver shall extend to any subsequent or other default or impair any right consequent thereon.

Section 6.7 Undertaking to Pay Costs.

All parties to this Indenture agree, and each holder of any Securities, by such holder's acceptance thereof shall be deemed to have agreed, that any court may in its discretion require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit, and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; provided, however, that the provisions of this Section 6.7 shall not apply to any suit instituted by the Trustee, to any suit instituted by any Securityholder, or group of Securityholders, holding more than 10% in aggregate principal amount of the Outstanding Securities of any series, or to any suit instituted by any Securityholder for the enforcement of the payment of the principal of (or premium, if any) or interest on any Security of such series, on or after the respective due dates expressed in such Security or established pursuant to this Indenture.

**ARTICLE VII
CONCERNING THE TRUSTEE**

Section 7.1 Certain Duties and Responsibilities of Trustee.

(a) The Trustee, prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing of all Events of Default with respect to the Securities of that series that may have occurred, shall undertake to perform with respect to the Securities of such series such duties and only such duties as are specifically set forth in this Indenture, and no implied covenants shall be read into this Indenture against the Trustee. In case an Event of Default with respect to the Securities of a series has occurred (that has not been cured or waived), the Trustee shall exercise with respect to Securities of that series such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in their exercise, as a prudent person would exercise or use under the circumstances in the conduct of such person's own affairs.

(b) No provision of this Indenture shall be construed to relieve the Trustee from liability for its own negligent action, its own negligent failure to act, or its own willful misconduct, except that:

(1) prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing or waiving of all such Events of Default with respect to that series that may have occurred:

(i) the duties and obligations of the Trustee shall with respect to the Securities of such series be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable with respect to the Securities of such series except for the performance of such duties and obligations as are specifically set forth in this Indenture, and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(ii) in the absence of bad faith on the part of the Trustee, the Trustee may, with respect to the Securities of such series, conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture; however, in the case of any such certificates or opinions that by any provision hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine whether or not they conform to the requirements of this Indenture;

(2) the Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer or Responsible Officers of the Trustee, unless it shall be proved that the Trustee was negligent in ascertaining the pertinent facts;

(3) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the direction of the holders of not less than a majority in principal amount of the Securities of any series at the time Outstanding (determined as provided in [Section 8.4](#)) relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee under this Indenture with respect to the Securities of that series; and

(4) none of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers, if there is reasonable ground for believing that the repayment of such funds or liability is not reasonably assured to it under the terms of this Indenture or adequate indemnity against such risk is not reasonably assured to it.

Section 7.2 Certain Rights of Trustee.

Except as otherwise provided in Section 7.1:

- (a) The Trustee may conclusively rely and shall be fully protected in acting or refraining from acting upon any document (whether in its original or facsimile form) believed by it to be genuine and to have been signed or presented by the proper Person. The Trustee need not investigate any fact or matter stated in the document. The Trustee shall receive and retain financial reports and statements of the Company as provided herein, but shall have no duty to review or analyze such reports or statements to determine compliance under covenants or other obligations of the Company.
- (b) Before the Trustee acts or refrains from acting, it may require an Officers' Certificate and an Opinion of Counsel, which shall conform to the provisions of Section 13.7. The Trustee shall not be liable for any action it takes or omits to take in good faith in reliance on such certificate or opinion.
- (c) The Trustee may act through its attorneys and agents, and shall not be responsible for the misconduct or negligence of any agent appointed with due care.
- (d) The Trustee shall not be required to give any bond or surety in respect of the performance of its powers and duties hereunder.
- (e) The permissive rights of the Trustee to take actions enumerated in this Indenture shall not be construed as duties.
- (f) Except with respect to Section 4.1, the Trustee shall have no duty to inquire as to the performance of the Company with respect to the covenants contained in Article Four. In addition, the Trustee shall not be deemed to have knowledge of an Event of Default, except (i) any Default or Event of Default occurring pursuant to Section 6.1(a)(2) or (ii) any Default or Event of Default of which a Responsible Officer of the Trustee shall have received written notification from the Company or any Holder of such Default or Event of Default at the Corporate Trust Office, and such notice references the applicable series of Securities and this Indenture.
- (g) The rights, privileges, protections, immunities and benefits given to the Trustee, including its right to be indemnified, are extended to, and shall be enforceable by, the Trustee in each of its capacities (including as Paying Agent) hereunder, and to each agent, custodian and other Person employed to act hereunder.
- (h) Delivery of reports, information and documents to the Trustee under Section 5.3 is for informational purposes only; the Trustee's receipt of the foregoing shall not constitute constructive notice of any information contained therein or determinable from information contained therein, including the Company's compliance with any of its covenants hereunder (as to which the Trustee is entitled to rely exclusively on an Officers' Certificate).

(i) The Trustee may request that the Company deliver an Officers' Certificate setting forth the names of individuals and/or titles of officers authorized at such time to take specified actions pursuant to this Indenture, which Officers' Certificate may be signed by any person authorized to sign an Officers' Certificate, including any person specified as so authorized in any such certificate previously delivered and not superseded.

(j) Anything in this Indenture notwithstanding, in no event shall the Trustee be liable for special, indirect, punitive or consequential loss or damage of any kind whatsoever (including but not limited to loss of profit), even if the Trustee has been advised as to the likelihood of such loss or damage and regardless of the form of action.

(k) The Trustee shall not be responsible or liable for any failure or delay in the performance of its obligations under this Indenture arising out of or caused, directly or indirectly, by circumstances beyond its reasonable control, including, without limitation, (i) acts of God, including earthquakes, fire and flood; (ii) terrorism, wars and other military disturbances; (iii) sabotage, epidemics and riots; (iv) interruptions, loss or malfunctions of utilities, computer (hardware or software) or communication services; (v) accidents and labor disputes; and (vi) acts of civil or military authorities and governmental actions.

Section 7.3 Trustee Not Responsible for Recitals or Issuance of Securities.

(a) The recitals contained herein and in the Securities shall be taken as the statements of the Company, and the Trustee assumes no responsibility for the correctness of the same.

(b) The Trustee makes no representations as to the validity or sufficiency of this Indenture or of the Securities.

(c) The Trustee shall not be accountable for the use or application by the Company of any of the Securities or of the proceeds of such Securities, or for the use or application of any moneys paid over by the Trustee in accordance with any provision of this Indenture or established pursuant to Section 2.1, or for the use or application of any moneys received by any paying agent other than the Trustee.

Section 7.4 May Hold Securities.

The Trustee or any paying agent or Security Registrar, in its individual or any other capacity, may become the owner or pledgee of Securities with the same rights it would have if it were not Trustee, paying agent or Security Registrar.

Section 7.5 Moneys Held in Trust.

Subject to the provisions of Section 11.5, all moneys received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received, but need not be segregated from other funds of the Trustee except to the extent required by law. The Trustee shall be under no liability for interest on any moneys received by it hereunder, except such as it may agree with the Company to pay thereon.

Section 7.6 Compensation and Reimbursement.

(a) The Company covenants and agrees to pay to the Trustee, and the Trustee shall be entitled to, such reasonable compensation (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust), as the Company and the Trustee may from time to time agree in writing, for all services rendered by it in the execution of the trusts hereby created and in the exercise and performance of any of the powers and duties hereunder of the Trustee. Except as otherwise expressly provided herein, the Company will pay or reimburse the Trustee upon its request for all reasonable expenses, disbursements and advances incurred or made by the Trustee in accordance with any of the provisions of this Indenture (including the reasonable compensation and the expenses and disbursements of its counsel and of all Persons not regularly in its employ). Except any such expense, disbursement or advance as may arise from its negligence or bad faith. The Company also covenants to indemnify the Trustee (and its officers, agents, directors and employees) for, and to hold it harmless against, any loss, liability or expense incurred without negligence or bad faith on the part of the Trustee and arising out of or in connection with the acceptance or administration of the trusts hereby created, including the reasonable costs and expenses of defending itself against any claim of liability in the premises.

(b) The obligations of the Company under this Section 7.6 to compensate and indemnify the Trustee and to pay or reimburse the Trustee for reasonable expenses, disbursements and advances shall constitute additional indebtedness hereunder. Such additional indebtedness shall be secured by a lien prior to that of the Securities upon all property and funds held or collected by the Trustee as such, except funds held in trust for the benefit of the holders of particular Securities. The provisions of this Section 7.6 shall survive the resignation or removal of the Trustee and the termination of this Indenture.

(c) When the Trustee incurs expenses or renders services after a Default specified in Section 6.1(a)(5) and (6) occurs, such expenses (including the charges and expenses of its counsel) and the compensation for such services shall be paid to the extent allowed under any Bankruptcy Law and are intended to constitute expenses of administration under any Bankruptcy Law.

Section 7.7 Reliance on Officers' Certificate.

Except as otherwise provided in Section 7.1, whenever in the administration of the provisions of this Indenture the Trustee shall deem it necessary or desirable that a matter be proved or established prior to taking or suffering or omitting to take any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of negligence or bad faith on the part of the Trustee, be deemed to be conclusively proved and established by an Officers' Certificate delivered to the Trustee and such certificate, in the absence of negligence or bad faith on the part of the Trustee, shall be full warrant to the Trustee for any action taken, suffered or omitted to be taken by it under the provisions of this Indenture upon the faith thereof.

Section 7.8 Disqualification; Conflicting Interests.

If the Trustee has or shall acquire any “conflicting interest” within the meaning of the Trust Indenture Act, the Trustee and the Company shall in all respects comply with the provisions of Section 310(b) of the Trust Indenture Act.

Section 7.9 Corporate Trustee Required; Eligibility.

There shall at all times be a Trustee with respect to the Securities issued hereunder, which shall at all times be a corporation organized and doing business under the laws of the United States of America or any state or territory thereof or of the District of Columbia, or a corporation or other Person permitted to act as trustee by the Securities and Exchange Commission, authorized under such laws to exercise corporate trust powers, having a combined capital and surplus of at least 50 million U.S. dollars (\$50,000,000), and subject to supervision or examination by federal, state, territorial or District of Columbia authority. If such corporation publishes reports of condition at least annually, pursuant to law or to the requirements of the aforesaid supervising or examining authority, then for the purposes of this Section 7.9, the combined capital and surplus of such corporation shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. The Company may not, nor may any Person directly or indirectly controlling, controlled by or under common control with the Company, serve as Trustee. In case at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section 7.9, the Trustee shall resign immediately in the manner and with the effect specified in Section 7.10.

Section 7.10 Resignation and Removal; Appointment of Successor.

(a) The Trustee or any successor hereafter appointed, may at any time resign with respect to the Securities of one or more series by giving written notice thereof to the Company and by transmitting notice of resignation electronically or by mail, first class postage prepaid, to the Securityholders of such series, as their names and addresses appear upon the Security Register. Upon receiving such notice of resignation, the Company shall promptly appoint a successor trustee with respect to the Securities of such series by or pursuant to a Board Resolution. If no successor trustee shall have been so appointed and have accepted such appointment within 30 days after the mailing of such notice of resignation, the resigning Trustee may petition any court of competent jurisdiction for the appointment of a successor trustee with respect to such Securities of such series, or any Securityholder of that series who has been a bona fide holder of a Security or Securities for at least six months may on behalf of himself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(b) In case at any time any one of the following shall occur:

(1) the Trustee shall fail to comply with the provisions of Section 7.8 after written request therefor by the Company or by any Securityholder who has been a bona fide holder of a Security or Securities for at least six months; or

(2) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.9 and shall fail to resign after written request therefor by the Company or by any such Securityholder; or

(3) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or commence a voluntary bankruptcy proceeding, or a receiver of the Trustee or of its property shall be appointed or consented to, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation, then, in any such case, the Company may remove the Trustee with respect to all Securities and appoint a successor trustee by or pursuant to a Board Resolution, or, unless the Trustee's duty to resign is stayed as provided herein, any Securityholder who has been a bona fide holder of a Security or Securities for at least six months may, on behalf of that holder and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(c) The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding may at any time remove the Trustee with respect to such series by so notifying the Trustee and the Company, and may appoint a successor Trustee for such series with the written consent of the Company.

(d) Any resignation or removal of the Trustee and appointment of a successor trustee with respect to the Securities of a series pursuant to any of the provisions of this Section 7.10 shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.11.

(e) Any successor trustee appointed pursuant to this Section 7.10 may be appointed with respect to the Securities of one or more series or all of such series, and at any time there shall be only one Trustee with respect to the Securities of any particular series.

Section 7.11 Acceptance of Appointment by Successor.

(a) In case of the appointment hereunder of a successor trustee with respect to all Securities, every such successor trustee so appointed shall execute, acknowledge and deliver to the Company and to the retiring Trustee an instrument accepting such appointment, and thereupon the resignation or removal of the retiring Trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee; however, upon the request of the Company or the successor trustee, such retiring Trustee shall, upon payment of its charges, execute and deliver an instrument transferring to such successor trustee all the rights, powers and trusts of the retiring Trustee and shall duly assign, transfer and deliver to such successor trustee all property and money held by such retiring Trustee hereunder.

(b) In case of the appointment hereunder of a successor trustee with respect to the Securities of one or more (but not all) series, the Company, the retiring Trustee and each successor trustee with respect to the Securities of one or more series shall execute and deliver an indenture supplemental hereto wherein each successor trustee shall accept such appointment and which (1) shall contain such provisions as shall be necessary or desirable to transfer and confirm to, and to vest in, each successor trustee all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates, (2) shall contain such provisions as shall be deemed necessary or desirable to confirm that all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series as to which the retiring Trustee is not retiring shall continue to be vested in the retiring Trustee and (3) shall add to or change any of the provisions of this Indenture as shall be necessary to provide for or facilitate the administration of the trusts hereunder by more than one Trustee, it being understood that nothing herein or in such supplemental indenture shall constitute such Trustees co-trustees of the same trust, that each such Trustee shall be trustee of a trust or trusts hereunder separate and apart from any trust or trusts hereunder administered by any other such Trustee and that no Trustee shall be responsible for any act or failure to act on the part of any other Trustee hereunder. The execution and delivery of such supplemental indenture, the resignation or removal of the retiring Trustee shall become effective to the extent provided therein, such retiring Trustee shall with respect to the Securities of that or those series to which the appointment of such successor trustee relates have no further responsibility for the exercise of rights and powers or for the performance of the duties and obligations vested in the Trustee under this Indenture, and each such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates; however, upon request of the Company or any successor trustee, such retiring Trustee shall duly assign, transfer and deliver to such successor trustee, to the extent contemplated by such supplemental indenture, the property and money held by such retiring Trustee hereunder with respect to the Securities of that or those series to which the appointment of such successor trustee relates.

(c) Upon request of any such successor trustee, the Company shall execute any and all instruments for more fully and certainly vesting in and confirming to such successor trustee all such rights, powers and trusts referred to in paragraph (a) or (b) of this Section 7.11, as the case may be.

(d) No successor trustee shall accept its appointment unless at the time of such acceptance such successor trustee shall be qualified and eligible under this Article.

(e) Upon acceptance of appointment by a successor trustee as provided in this Section 7.11, the Company shall transmit notice of the succession of such trustee hereunder by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register. If the Company fails to transmit such notice within ten days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be transmitted at the expense of the Company.

Section 7.12 Merger, Conversion, Consolidation or Succession to Business.

Any corporation into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation succeeding to the corporate trust business of the Trustee, shall be the successor of the Trustee hereunder, provided that such corporation shall be qualified under the provisions of Section 7.8 and eligible under the provisions of Section 7.9, without the execution or filing of any paper or any further act on the part of any of the parties hereto, anything herein to the contrary notwithstanding. In case any Securities shall have been authenticated, but not delivered, by the Trustee then in office, any successor by merger, conversion or consolidation to such authenticating Trustee may adopt such authentication and deliver the Securities so authenticated with the same effect as if such successor Trustee had itself authenticated such Securities.

Section 7.13 Preferential Collection of Claims Against the Company.

The Trustee shall comply with Section 311(a) of the Trust Indenture Act, excluding any creditor relationship described in Section 311(b) of the Trust Indenture Act. A Trustee who has resigned or been removed shall be subject to Section 311(a) of the Trust Indenture Act to the extent included therein.

Section 7.14 Notice of Defaults.

If a Default occurs and is continuing hereunder with respect to Securities of any series and if it is actually known to a Responsible Officer of the Trustee, the Trustee shall send to each holder of such Securities notice of the Default within 90 days after such Default occurs provided, however, that in the case of any Default of the character specified in Section 6.1(a)(3) with respect to Securities of such series, no such notice to Holders shall be given until at least 30 days after the occurrence thereof. Except in the case of a default in payment of principal of or interest on any Security (whether upon redemption, repurchase, maturity or otherwise) (including payments pursuant to the redemption or repurchase provisions of such Security, if any) or payment or delivery of any amounts due upon conversion of Securities of any series that are convertible into shares of common stock or other securities, the Trustee may withhold the notice if and so long as a committee of its Responsible Officers in good faith determines that withholding the notice is in the interests of the holders of such Securities.

**ARTICLE VIII
CONCERNING THE SECURITYHOLDERS**

Section 8.1 Evidence of Action by Securityholders.

Whenever in this Indenture it is provided that the holders of a majority or specified percentage in aggregate principal amount of the Securities of a particular series may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action the holders of such majority or specified percentage of that series have joined therein may be evidenced by any instrument or any number of instruments of similar tenor executed by such holders of Securities of that series in Person or by agent or proxy appointed in writing.

If the Company shall solicit from the Securityholders of any series any request, demand, authorization, direction, notice, consent, waiver or other action, the Company may, at its option, as evidenced by an Officers' Certificate, fix in advance a record date (in accordance with Section 316(c) of the Trust Indenture Act) for such series for the determination of Securityholders entitled to give such request, demand, authorization, direction, notice, consent, waiver or other action, but the Company shall have no obligation to do so. If such a record date is fixed, such request, demand, authorization, direction, notice, consent, waiver or other action may be given before or after the record date, but only the Securityholders of record at the close of business on the record date shall be deemed to be Securityholders for the purpose of determining whether Securityholders of the requisite proportion of Outstanding Securities of that series have authorized or agreed or consented to such request, demand, authorization, direction, notice, consent, waiver or other action, and for that purpose the Outstanding Securities of that series shall be computed as of the record date; provided, however, that no such authorization, agreement or consent by such Securityholders on the record date shall be deemed effective unless it shall become effective pursuant to the provisions of this Indenture not later than six months after the record date.

Section 8.2 Proof of Execution by Securityholders.

Subject to the provisions of Section 7.1, proof of the execution of any instrument by a Securityholder (such proof will not require notarization) or his or her agent or proxy and proof of the holding by any Person of any of the Securities shall be sufficient if made in the following manner:

- (a) The fact and date of the execution by any such Person of any instrument may be proved in any reasonable manner acceptable to the Company.
- (b) The ownership of Securities shall be proved by the Security Register of such Securities or by a certificate of the Security Registrar thereof.
- (c) The Trustee or the Company may require such additional proof of any matter referred to in this Section 8.2 as it shall deem necessary.

Section 8.3 Who May be Deemed Owners.

Prior to the due presentment for registration of transfer of any Security, the Company, the Trustee, any paying agent and any Security Registrar may deem and treat the Person in whose name such Security shall be registered upon the books of the Company as the absolute owner of such Security (whether or not such Security shall be overdue and notwithstanding any notice of ownership or writing thereon made by anyone other than the Security Registrar) for the purpose of receiving payment of or on account of the principal of, premium, if any, and (subject to Section 2.3) interest on such Security and for all other purposes. Neither the Company nor the Trustee nor any paying agent nor any Security Registrar shall be affected by any notice to the contrary.

Section 8.4 Certain Securities Owned by Company Disregarded.

In determining whether the holders of the requisite aggregate principal amount of Securities of a particular series have concurred in any direction or consent (or waiver, as the case may be) under this Indenture, the Securities of that series that are owned by the Company or any other obligor on the Securities of that series, or by any Person directly or indirectly controlling or controlled by or under direct or indirect common control with the Company or any other obligor on the Securities of that series, shall be disregarded and deemed not to be Outstanding for the purpose of any such determination, except that for the purpose of determining whether the Trustee shall be protected in relying on any such direction or consent (or waiver, as the case may be), only Securities of such series that the Trustee actually knows are so owned shall be so disregarded. The Securities so owned that have been pledged in good faith may be regarded as Outstanding for the purposes of this Section 8.4, if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right so to act with respect to such Securities and that the pledgee is not a Person directly or indirectly controlling or controlled by or under direct or indirect common control with the Company or any such other obligor. In case of a dispute as to such right, any decision by the Trustee taken upon the advice of counsel shall be full protection to the Trustee.

Section 8.5 Actions Binding on Future Securityholders.

At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.1, of the taking of any action by the holders of the majority or percentage in aggregate principal amount of the Securities of a particular series specified in this Indenture in connection with such action, any holder of a Security of that series that is shown by the evidence to be included in the Securities the holders of which have consented to such action may, by filing written notice with the Trustee, and upon proof of holding as provided in Section 8.2, revoke such action so far as concerns such Security. Except as aforesaid, any such action taken by the holder of any Security shall be conclusive and binding upon such holder and upon all future holders and owners of such Security, and of any Security issued in exchange therefor, on registration of transfer thereof or in place thereof, irrespective of whether or not any notation in regard thereto is made upon such Security. Any action taken by the holders of the majority or percentage in aggregate principal amount of the Securities of a particular series specified in this Indenture in connection with such action shall be conclusively binding upon the Company, the Trustee and the holders of all the Securities of that series.

**ARTICLE IX
SUPPLEMENTAL INDENTURES**

Section 9.1 Supplemental Indentures Without the Consent of Securityholders.

In addition to any supplemental indenture otherwise authorized by this Indenture, the Company and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect), without the consent of the Securityholders, for one or more of the following purposes:

- (a) to cure any ambiguity, omission, defect or inconsistency herein or in the Securities of any series;
- (b) to comply with Article Ten;
- (c) to provide for Securities in bearer form, or uncertificated Securities in addition to or in place of certificated Securities;

- (d) to add Guarantees, including Subsidiary Guarantees, with respect to debt securities or to release Subsidiary Guarantors from Subsidiary Guarantees in accordance with the terms of the applicable series of Securities or to secure a series of Securities;
- (e) to add to the covenants of the Company for the benefit of the holders of all or any series of Securities (and if such covenants are to be for the benefit of less than all series of Securities, stating that such covenants are expressly being included solely for the benefit of such series) or to surrender any right or power herein conferred upon the Company;
- (f) to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms or purposes of issue, authentication and delivery of Securities, as herein set forth;
- (g) to make any change that does not adversely affect the rights of any Securityholder in any material respect, provided that any amendment to conform the terms of any Securities to its description contained in the final offering document shall not be deemed to be adverse to any Securityholder;
- (h) to provide for the issuance of and establish the form and terms and conditions of the Securities of any series as provided in Section 2.1, to establish the form of any certifications required to be furnished under the terms of this Indenture or any series of Securities, or to add to the rights of the holders of any series of Securities;
- (i) to comply with any requirements of the Securities and Exchange Commission in connection with registration of the Securities under the Securities Act qualifying, or maintaining the qualification of, this Indenture under the Trust Indenture Act or to comply with the Trust Indenture Act; or
- (j) to secure any series of Security.

The Trustee is hereby authorized to join with the Company in the execution of any such supplemental indenture, and to make any further appropriate agreements and stipulations that may be therein contained, but the Trustee shall not be obligated to enter into any such supplemental indenture that affects the Trustee's own rights, duties or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section 9.1 may be executed by the Company and the Trustee without the consent of the holders of any of the Securities at the time Outstanding, notwithstanding any of the provisions of Section 9.2.

Section 9.2 Supplemental Indentures with Consent of Securityholders.

With the consent (evidenced as provided in Section 8.1) of the holders of not less than a majority in aggregate principal amount of the Securities of each series affected by such supplemental indenture or indentures at the time Outstanding, the Company, when authorized by Board Resolutions, and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect) for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or of any supplemental indenture or of modifying in any manner not covered by Section 9.1 the rights of the holders of the Securities of such series under this Indenture; provided, however, that no such supplemental indenture shall, without the consent of the holders of each Security then Outstanding affected thereby, (i) change the maturity date of any Securities of any series, or reduce the principal amount thereof, or reduce the rate or extend the time of payment of interest thereon, or reduce any premium payable upon the redemption thereof; (ii) reduce the amount of principal of an Original Issue Discount Security or any other Security payable upon acceleration of maturity; (iii) change the currency in which any Security or any premium or interest is payable; (iv) impair the right to receive payment of principal of and interest on any Security (whether upon redemption, repurchase, maturity, or otherwise) or payment or delivery of any amounts due upon conversion of Securities of any series that are convertible into shares of common stock or other securities on or after the due dates or to institute suit for the enforcement of any payment on or with respect to any Security; (v) adversely change the right to convert or exchange, including decreasing the conversion rate or increasing the conversion price of, that Security (if applicable); (vi) if the Securities are secured, change the terms and conditions pursuant to which the Securities are secured in a manner adverse to the holders of the Securities; (vii) reduce the percentage in principal amount of outstanding Securities of any series, the consent of whose holders is required for modification or amendment of this Indenture or for waiver of compliance with any provision of this Indenture; (viii) reduce the requirements contained in this Indenture for a quorum for a meeting or for voting; (ix) change any obligations of the Company to maintain an office or agency in the places and for the purposes required by this Indenture; or (x) modify any of the above provisions.

It shall not be necessary for the consent of the Securityholders of any series affected thereby under this Section 9.2 to approve the particular form of any proposed supplemental indenture, but it shall be sufficient if such consent shall approve the substance thereof.

Section 9.3 Effect of Supplemental Indentures.

Upon the execution of any supplemental indenture pursuant to the provisions of this Article or of Section 10.1, this Indenture shall, with respect to such series, be deemed to be modified and amended in accordance therewith and the respective rights, limitations of rights, obligations, duties and immunities under this Indenture of the Trustee, the Company and the holders of Securities of the series affected thereby shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments, and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 9.4 Securities Affected by Supplemental Indentures.

Securities of any series affected by a supplemental indenture, authenticated and delivered after the execution of such supplemental indenture pursuant to the provisions of this Article or of Section 10.1, may bear a notation in form approved by the Company, provided such form meets the requirements of any exchange upon which such series may be listed, as to any matter provided for in such supplemental indenture. If the Company shall so determine, new Securities of that series so modified as to conform, in the opinion of the Trustee and the Company, to any modification of this Indenture contained in any such supplemental indenture may be prepared and executed by the Company, authenticated by the Trustee and delivered in exchange for the Securities of that series then Outstanding.

Section 9.5 Execution of Supplemental Indentures.

Upon the request of the Company, accompanied by the Board Resolutions authorizing the execution of any such supplemental indenture, and upon the filing with the Trustee of evidence of the consent of Securityholders required to consent thereto as aforesaid, the Trustee shall join with the Company in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may, in its discretion (but without any obligation to do so) enter into such supplemental indenture. The Trustee, subject to the provisions of Section 7.1, shall be provided an Opinion of Counsel and an Officers' Certificate as conclusive evidence that any supplemental indenture executed pursuant to this Article is authorized or permitted by, and conforms to, the terms of this Article and that it is proper for the Trustee under the provisions of this Article to join in the execution thereof; provided, however, that such Opinion of Counsel need not be provided in connection with the execution of a supplemental indenture that establishes the terms of a series of Securities pursuant to Section 2.1 hereof, unless otherwise requested by the Trustee.

Section 9.6 Conformity with Trust Indenture Act.

Every supplemental indenture executed pursuant to this Article shall conform to the requirements of the Trust Indenture Act in effect on such date.

ARTICLE X
SUCCESSOR CORPORATION

Section 10.1 Company May Consolidate, Etc.

Unless otherwise specified in a supplemental indenture hereto, nothing contained in this Indenture or in any of the Securities shall prevent any consolidation or merger of the Company with or into any other Person (whether or not affiliated with the Company) or successive consolidations or mergers in which the Company or its successor or successors shall be a party or parties, or shall prevent any sale, conveyance, transfer or other disposition of the property of the Company or its successor or successors as an entirety, or substantially as an entirety, to any other Person (whether or not affiliated with the Company or its successor or successors) authorized to acquire and operate the same. The Company hereby covenants and agrees that, upon any such consolidation or merger (in each case, if the Company is not the surviving corporation of such transaction), sale, conveyance, transfer or other disposition, the due and punctual payment of the principal of and any premium and interest on all of the Securities of all series in accordance with the terms of each series, according to their tenor and the due and punctual performance and observance of all the covenants and conditions of this Indenture with respect to each series or established with respect to such series pursuant to Section 2.1 to be kept or performed by the Company shall be expressly assumed, by supplemental indenture (which shall conform to the requirements of the Trust Indenture Act as then in effect) satisfactory in form to the Trustee executed and delivered to the Trustee by the entity formed by such consolidation, or into which the Company shall have been merged, or by the entity which shall have acquired such property.

Section 10.2 Successor Substituted.

(a) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition and upon the assumption by the successor Person, by supplemental indenture, executed and delivered to the Trustee and satisfactory in form to the Trustee, of the due and punctual payment of the principal of and any premium and interest on all of the Securities of all series Outstanding and the due and punctual performance of all of the covenants and conditions of this Indenture or established with respect to each series of the Securities pursuant to Section 2.1 to be performed by the Company with respect to each series, such successor Person shall succeed to and be substituted for the Company with the same effect as if it had been named as the Company herein, and thereupon the predecessor Person shall be relieved of all obligations and covenants under this Indenture and the Securities.

(b) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition such changes in phraseology and form (but not in substance) may be made in the Securities thereafter to be issued as may be appropriate.

(c) Nothing contained in this Indenture or in any of the Securities shall prevent the Company from merging into itself or acquiring by purchase or otherwise all or any part of the property of any other Person (whether or not affiliated with the Company).

Section 10.3 Evidence of Consolidation, Etc. to Trustee.

The Trustee, subject to the provisions of Section 7.1, shall be provided an Opinion of Counsel and an Officers' Certificate as conclusive evidence that any such consolidation, merger, sale, conveyance, transfer or other disposition, and any such assumption, comply with the provisions of this Article.

ARTICLE XI
SATISFACTION AND DISCHARGE

Section 11.1 Satisfaction and Discharge of Indenture.

If at any time: (a) the Company shall have delivered to the Trustee for cancellation all Securities of a series theretofore authenticated (other than any Securities that shall have been destroyed, lost or stolen and that shall have been replaced or paid as provided in Section 2.7 and Securities for whose payment money or Governmental Obligations have theretofore been deposited in trust or segregated and held in trust by the Company and thereupon repaid to the Company or discharged from such trust, as provided in Section 11.5); or (b) all such Securities of a particular series not theretofore delivered to the Trustee for cancellation shall have become due and payable, or, except in the case of any Securities that are convertible or exchangeable, are by their terms to become due and payable within one year or are to be called for redemption within one year under arrangements satisfactory to the Trustee for the giving of notice of redemption, and the Company shall deposit or cause to be deposited with the Trustee as trust funds an amount of money in U.S. dollars sufficient, or non-callable Governmental Obligations, the principal of and interest on which when due, will be sufficient or a combination thereof, sufficient in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, to pay at maturity or upon redemption all Securities of that series not theretofore delivered to the Trustee for cancellation, including principal and any premium and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder with respect to such series by the Company then this Indenture shall thereupon cease to be of further effect with respect to such series except for the provisions of Sections 2.3, 2.5, 2.7, 4.1, 4.2, 4.3 and 7.10, that shall survive until the date of maturity or redemption date, as the case may be, and Sections 7.6 and 11.5, that shall survive to such date and thereafter, and the Trustee, on demand of the Company and at the cost and expense of the Company shall execute proper instruments acknowledging satisfaction of and discharging this Indenture with respect to such series.

Section 11.2 Discharge of Obligations.

If at any time all such Securities of a particular series not heretofore delivered to the Trustee for cancellation or that have not become due and payable as described in Section 11.1 shall have been paid by the Company by depositing irrevocably with the Trustee as trust funds money in U.S. dollars sufficient or an amount of non-callable Governmental Obligations, the principal of and interest on which when due, will be sufficient or a combination thereof, sufficient in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, to pay at maturity or upon redemption all such Securities of that series not theretofore delivered to the Trustee for cancellation, including principal and any premium and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder by the Company with respect to such series, then after the date such moneys or Governmental Obligations, as the case may be, are deposited with the Trustee the obligations of the Company under this Indenture with respect to such series shall cease to be of further effect except for the provisions of Sections 2.3, 2.5, 2.7, 4.1, 4.2, 4.3, 7.6, 7.10 and 11.5 hereof that shall survive until such Securities shall mature and be paid. Thereafter, Sections 7.6 and 11.5 shall survive.

Section 11.3 Deposited Moneys to be Held in Trust.

All moneys or Governmental Obligations deposited with the Trustee pursuant to Sections 11.1 or 11.2 shall be held in trust and shall be available for payment as due, either directly or through any paying agent (including the Company acting as its own paying agent), to the holders of the particular series of Securities for the payment or redemption of which such moneys or Governmental Obligations have been deposited with the Trustee.

Section 11.4 Payment of Moneys Held by Paying Agents.

In connection with the satisfaction and discharge of this Indenture, all moneys or Governmental Obligations then held by any paying agent under the provisions of this Indenture shall, upon demand of the Company, be paid to the Trustee, and thereupon such paying agent shall be released from all further liability with respect to such moneys or Governmental Obligations.

Section 11.5 Repayment to Company.

Any moneys or Governmental Obligations deposited with any paying agent or the Trustee, or then held by the Company, in trust for payment of principal of or premium or interest on the Securities of a particular series that are not applied but remain unclaimed by the holders of such Securities for at least two years after the date upon which the principal of and any premium or interest on such Securities shall have respectively become due and payable, shall be repaid to the Company or (if then held by the Company) shall be discharged from such trust. The paying agent and the Trustee thereupon shall be released from all further liability with respect to such moneys or Governmental Obligations, and the holder of any of the Securities entitled to receive such payment shall thereafter, as an unsecured general creditor, look only to the Company for the payment thereof.

ARTICLE XII
IMMUNITY OF INCORPORATORS, STOCKHOLDERS, OFFICERS AND DIRECTORS

Section 12.1 No Recourse.

No recourse under or upon any obligation, covenant or agreement of this Indenture, or of any Security, or for any claim based thereon or otherwise in respect thereof, shall be had against any incorporator, stockholder, officer or director, past, present or future as such, of the Company or of any predecessor or successor corporation, either directly or through the Company or any such predecessor or successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise, it being expressly understood that this Indenture and the obligations issued hereunder are solely corporate obligations, and that no such personal liability whatever shall attach to, or is or shall be incurred by, the incorporators, stockholders, officers or directors as such, of the Company or of any predecessor or successor corporation, or any of them, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom. Any and all such personal liability of every name and nature, either at common law or in equity or by constitution or statute, of, and any and all such rights and claims against, every such incorporator, stockholder, officer or director as such, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom, are hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issuance of such Securities.

ARTICLE XIII
MISCELLANEOUS PROVISIONS

Section 13.1 Effect on Successors and Assigns.

All the covenants, stipulations, promises and agreements in this Indenture contained by or on behalf of the Company shall bind its successors and assigns, whether so expressed or not.

Section 13.2 Actions by Successor.

Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or officer of the Company shall and may be done and performed with like force and effect by the corresponding board, committee or officer of any Person that shall at the time be the lawful sole successor of the Company.

Section 13.3 Notices.

Except as otherwise expressly provided herein, any notice or demand that by any provision of this Indenture is required or permitted to be given or served by the Trustee or by the holders of Securities to or on the Company may be given or served by being deposited first class postage prepaid in a post-office letterbox addressed (until another address is filed in writing by the Company with the Trustee), as follows: Cycleron Therapeutics, Inc., 301 Binney Street, Cambridge, Massachusetts 02142, Attention: Chief Financial Officer. Any notice, election, request or demand by the Company or any Securityholder to or upon the Trustee shall be deemed to have been sufficiently given or made, for all purposes, if given or made in writing at the Corporate Trust Office of the Trustee.

Section 13.4 Notice to Holders of Securities; Waiver.

Except as otherwise expressly provided herein, where this Indenture provides for notice to holders of Securities of any event, such notice shall be sufficiently given to holders of Securities if in writing and mailed, first-class postage prepaid, to each holder of a Security affected by such event, at the address of such holder as it appears in the Security Register, not earlier than the earliest date, and not later than the latest date, prescribed for the giving of such notice.

In case by reason of the suspension of regular mail service or by reason of any other cause it shall be impracticable to give such notice to holders of Securities by mail, then such notification as shall be made with the approval of the Trustee shall constitute sufficient notice to such holder for every purpose hereunder. In any case where notice to holders of Securities is given by mail, neither the failure to mail such notice, nor any defect in any notice mailed to any particular holder of a Security shall affect the sufficiency of such notice with respect to other holders of Securities given as provided herein.

Where this Indenture provides for notice in any manner, such notice may be waived in writing by the Person entitled to receive such notice, either before or after the applicable event, and such waiver shall be the equivalent of such notice. Waivers of notice by holders of Securities shall be filed with the Trustee, but such filing shall not be a condition precedent to the validity of any action taken in reliance upon such waiver.

Section 13.5 Governing Law.

This Indenture and each Security shall be deemed to be a contract made under the internal laws of the State of New York, and for all purposes shall be construed in accordance with the laws of said State.

Section 13.6 Effect of Headings and Table of Contents.

The Article and Section headings herein and the Table of Contents are for convenience only and shall not affect the construction hereof.

Section 13.7 Compliance Certificates and Opinions.

(a) Upon any application or demand by the Company to the Trustee to take any action under any of the provisions of this Indenture, the Company shall furnish to the Trustee an Officers' Certificate stating that all conditions precedent provided for in this Indenture relating to the proposed action have been complied with and an Opinion of Counsel stating that in the opinion of such counsel all such conditions precedent have been complied with. However, in the case of any such application or demand as to which the furnishing of such documents is specifically required by any provision of this Indenture relating to such particular application or demand, no additional certificate or opinion need be furnished.

(b) Each certificate or opinion provided for in this Indenture and delivered to the Trustee with respect to compliance with a condition or covenant in this Indenture shall include (i) a statement that the Person making such certificate or opinion has read such covenant or condition; (ii) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such certificate or opinion are based; (iii) a statement that, in the opinion of such Person, he has made such examination or investigation as is necessary to enable him to express an informed opinion as to whether or not such covenant or condition has been complied with; and (iv) a statement as to whether or not, in the opinion of such Person, such condition or covenant has been complied with. Each opinion delivered to the Trustee hereunder may rely on the facts stated in an Officers' Certificate delivered therewith.

Section 13.8 Payments on Business Days.

Except as provided pursuant to Section 2.1 pursuant to a Board Resolution, and as set forth in an Officers' Certificate, or established in one or more indentures supplemental to this Indenture, in any case where the date of maturity of interest or principal of any Security or the date of redemption or repurchase of any Security shall not be a Business Day, then payment of interest or principal (and premium, if any) (whether upon repurchase, redemption, maturity, or otherwise) may be made on the next succeeding Business Day with the same force and effect as if made on the nominal date of maturity, redemption, or repurchase, and no additional interest shall accrue for the period after such nominal date.

Section 13.9 Conflict with Trust Indenture Act.

If and to the extent that any provision of this Indenture limits, qualifies or conflicts with the duties imposed by Sections 310 to 317, inclusive, of the Trust Indenture Act, such imposed duties shall control.

Section 13.10 Counterparts.

This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument.

Section 13.11 Separability.

In case any one or more of the provisions contained in this Indenture or in the Securities of any series shall for any reason be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Indenture or of such Securities, but this Indenture and such Securities shall be construed as if such invalid or illegal or unenforceable provision had never been contained herein or therein.

Section 13.12 Assignment.

The Company will have the right at all times to assign any of its rights or obligations under this Indenture to a direct or indirect wholly-owned Subsidiary of the Company, provided that, in the event of any such assignment, the Company, will remain liable for all such obligations. Subject to the foregoing, the Indenture is binding upon and inures to the benefit of the parties thereto and their respective successors and assigns. This Indenture may not otherwise be assigned by the parties thereto.

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed all as of the day and year first above written.

CYCLERION THERAPEUTICS, INC.

By _____
Name:
Title:

As Trustee

By _____
Name:
Title:

July 24, 2020

Cyclerion Therapeutics, Inc.
301 Binney Street
Cambridge, Massachusetts 02142

RE: Cyclerion Therapeutics, Inc.
Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Cyclerion Therapeutics, Inc., a Massachusetts corporation (the "Company"), in connection with the filing today by the Company of a registration statement on Form S-3 (the "Registration Statement") under the Securities Act of 1933, as amended (the "Securities Act"). The Registration Statement registers the following securities of the Company: (i) shares of common stock of the Company, no par value per share (the "Common Stock"), (ii) shares of preferred stock of the Company, no par value per share (the "Preferred Stock"), (iii) debt securities of the Company (the "Debt Securities"), including those initially issuable upon exercise of any Warrants (as defined below) that are exercisable for Debt Securities; (iv) warrants of the Company (the "Warrants") to purchase Common Stock, Preferred Stock or Debt Securities, and (v) units of the Company (the "Units") consisting of Common Stock, Preferred Stock, Debt Securities and/or Warrants. The Debt Securities, the Warrants and the Units are collectively referred to as the "Securities".

This opinion is being furnished in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act.

In rendering the opinions stated herein, we have examined and relied upon the following:

- (a) the Registration Statement relating to the Common Stock, Preferred Stock, Debt Securities, Warrants and Units filed on the date hereof with the Securities and Exchange Commission (the "Commission") under the Securities Act;
- (b) an executed copy of a certificate of William Huyett, the Chief Financial Officer of the Company, dated the date hereof (the "Officer's Certificate"); and
- (c) a copy of certain resolutions (the "Resolutions") of the Board of Directors of the Company, adopted on July 20, 2020, certified pursuant to the Officer's Certificate.

We have also examined originals or copies, certified or otherwise identified to our satisfaction, of such records of the Company and such agreements, certificates and receipts of public officials, certificates of officers or other representatives of the Company and others, and such other documents as we have deemed necessary or appropriate as a basis for the opinions stated below.

In our examination, we have assumed the genuineness of all signatures, including endorsements, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as facsimile, electronic, certified or photostatic copies, and the authenticity of the originals of such copies. As to any facts relevant to the opinions stated herein that we did not independently establish or verify, we have relied upon statements and representations of officers and other representatives of the Company and others and of public officials, including those in the Officer's Certificate.

We do not express any opinion with respect to any laws other than the laws of the State of New York (the foregoing being referred to as "Opined-on Law").

Based upon the foregoing and subject to the qualifications and assumptions stated herein, we are of the opinion that:

(1) *Debt Securities*. When the Registration Statement has become effective under the Securities Act, the terms of an indenture under which any Debt Securities are to be issued have been duly established and such indenture has been duly authorized, executed and delivered, the terms of such Debt Securities and of their issuance and sale have been duly established in conformity with the applicable indenture and applicable law and such Debt Securities have been duly executed and authenticated in accordance with the applicable indenture and applicable law and issued and sold as contemplated by the Registration Statement, and if all the foregoing actions are taken pursuant to the authority granted in the Resolutions and so as not to violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and so as to comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, such Debt Securities will constitute valid and legally binding obligations of the Company, subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws of general applicability relating to or affecting creditors' rights and to general equity principles. The Debt Securities covered by the opinion in this paragraph include any Debt Securities issuable upon exercise of any Warrants that are exercisable for Debt Securities.

(2) *Warrants*. When the Registration Statement has become effective under the Securities Act, the terms of a warrant agreement under which any Warrants are to be issued have been duly established and such warrant agreement has been duly authorized, executed and delivered, the terms of such Warrants and of their issuance and sale have been duly established in conformity with the applicable warrant agreement and applicable law and such Warrants have been duly executed and authenticated in accordance with the applicable warrant agreement and applicable law and issued and sold as contemplated by the Registration Statement, and if all the foregoing actions are taken pursuant to the authority granted in the Resolutions and so as not to violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and so as to comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, such Warrants will constitute valid and legally binding obligations of the Company, subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws of general applicability relating to or affecting creditors' rights and to general equity principles.

(3) *Units*. When the Registration Statement has become effective under the Securities Act, the terms of a unit agreement under which any Units are to be issued have been duly established and such unit agreement has been duly authorized, executed and delivered, the terms of such Units and of their issuance and sale have been duly established in conformity with the applicable unit agreement and applicable law and such Units have been duly executed and authenticated in accordance with the applicable unit agreement and applicable law and issued and sold as contemplated by the Registration Statement, and if all the foregoing actions are taken pursuant to the authority granted in the Resolutions and so as not to violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and so as to comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, such Units will constitute valid and legally binding obligations of the Company, subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and similar laws of general applicability relating to or affecting creditors' rights and to general equity principles.

In rendering the foregoing opinions we have assumed that:

(a) Neither the issuance nor sale of the Debt Securities, Warrants and Units: (i) constitutes or will constitute a violation of, or a default under, any lease, indenture, instrument or other agreement to which the Company or its property is subject (except that we do not make the assumption set forth in this clause (i) with respect to those agreements or instruments which are listed in Part II of the Registration Statement), (ii) contravenes or will contravene any order or decree of any governmental authority to which the Company or its property is subject, or (iii) violates or will violate any law, rule or regulation to which the Company or its property is subject (except that we do not make the assumption set forth in this clause (iii) with respect to the Opined-on Law); and

(b) neither the issuance nor sale of the Debt Securities, Warrants and Units requires or will require the consent, approval, licensing or authorization of, or any filing, recording or registration with, any governmental authority under any law, rule or regulation of any jurisdiction (except that we do not make the assumption set forth in this clause (b) with respect to the Opined-on Law).

This opinion is limited to the specific issues addressed herein, and no opinion may be inferred or implied beyond that expressly stated herein. We assume no obligation to revise or supplement this opinion should the law of the State of New York be changed by legislative action, judicial decision or otherwise.

This opinion is furnished to you in connection with the filing of the Registration Statement and is not to be used, circulated, quoted or otherwise relied upon for any other purposes.

We hereby consent to the reference to our firm under the heading "Legal Matters" in the prospectus forming part of the Registration Statement. We also hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement. In giving this consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Hughes Hubbard & Reed LLP

Seaport West
155 Seaport Boulevard
Boston, MA 02210-2600

617 832 1000 *main*
617 832 7000 *fax*

July 24, 2020

Cyclerion Therapeutics, Inc.
301 Binney Street
Cambridge, Massachusetts 02142

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as special Massachusetts counsel to Cyclerion Therapeutics, Inc., a Massachusetts corporation (the “**Company**”), in connection with its filing of a registration statement on Form S-3 (the “**Registration Statement**”) with the Securities and Exchange Commission (the “**Commission**”) under the Securities Act of 1933, as amended (the “**Securities Act**”), on the date hereof.

The Registration Statement includes a base prospectus (the “**Prospectus**”), which provides that it will be supplemented in the future by one or more supplements to the Prospectus describing the securities offered thereby and the terms of the offering (each, a “**Prospectus Supplement**”). The Prospectus provides for the offer and sale of up to \$150,000,000 in aggregate offering price of the following securities: (i) shares of the Company’s common stock, no par value per share (“**Common Stock**”), (ii) shares of one or more series of the Company’s preferred stock, no par value per share (“**Preferred Stock**”), (iii) one or more series of the Company’s debt securities, which may be issued pursuant to an indenture between the Company, as issuer, and a trustee to be named therein (the “**Trustee**”), in the form filed as Exhibit 4.2 to the Registration Statement (as such indenture may be amended or supplemented from time to time, the “**Indenture**”), and one or more supplements or officer’s certificates thereto or resolutions of the Board of Directors of the Company, in each case establishing the terms of each such series (collectively, “**Debt Securities**”), (iv) warrants to purchase Common Stock, Preferred Stock, Debt Securities or any combination of the foregoing (“**Warrants**”), and (v) units consisting of Common Stock, Preferred Stock, Debt Securities and/or Warrants, which may or may not be separable from one another (“**Units**”). The Common Stock, Preferred Stock, Debt Securities, Warrants and Units are collectively referred to as the “**Securities**.”

The Debt Securities may be exchangeable and/or convertible into other Securities. The Warrants may be issued under one or more warrant agreements (each, a “**Warrant Agreement**”) between the Company and a third party to be identified therein as warrant agent. The Units may be issued under one or more unit agreements (each, a “**Unit Agreement**”) between the Company and a third party to be identified therein as unit agent. The Indenture, the Warrant Agreements and the Unit Agreements are herein collectively referred to as the “**Agreements**.”

The Securities may be offered and sold from time to time pursuant to Rule 415 promulgated under the Securities Act, in amounts, at prices and on terms to be determined at the time of the offering thereof.

We have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. We have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We have assumed that the proceedings to be taken by the Company after the date hereof in connection with the authorization of the Agreements and the authorization, issuance and sale of the Securities, and the terms of each issuance, will be in compliance with law. In our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals and the conformity to authentic original documents of all documents submitted to us as copies.

The opinions expressed below are limited to the internal laws of the Commonwealth of Massachusetts.

Subject to the foregoing and the other matters set forth herein, it is our opinion that, as of the date hereof:

1. When an issuance of shares of Common Stock has been duly authorized by all necessary corporate action of the Company and the Board of Directors of the Company has determined that the consideration to be received for such shares is adequate, upon issuance, delivery and payment of such consideration therefor in the manner contemplated by the Registration Statement, the Prospectus and the applicable Prospectus Supplement(s), by such corporate action and by the terms of any underwriting, purchase or other agreement, instrument or Security relating to such issuance, such shares of Common Stock will be validly issued, fully paid and nonassessable.

2. When a series of Preferred Stock has been duly authorized and established in accordance with the Massachusetts Business Corporation Act and the terms of the Company's Restated Articles of Organization, an issuance of shares of such series of Preferred Stock has been duly authorized by all necessary corporate action of the Company and the Board of Directors of the Company has determined that the consideration to be received for such shares is adequate, upon issuance, delivery and payment of such consideration therefor in the manner contemplated by the Registration Statement, the Prospectus and the applicable Prospectus Supplement(s), by such corporate action and by the terms of any underwriting, purchase or other agreement, instrument or Security relating to such issuance, such shares of Preferred Stock will be validly issued, fully paid and nonassessable.

3. The Company has the corporate power to enter into the Indenture and to issue and sell Debt Securities thereunder and, when the Board of Directors of the Company has taken all necessary corporate action to authorize the Indenture, establish the specific terms of a particular series of Debt Securities in accordance with the Indenture and authorize the issuance and sale of such Debt Securities, the Company will have the authority to execute and deliver the Indenture and to execute, issue and deliver such Debt Securities.

4. The Company has the corporate power to enter into a Warrant Agreement and to issue and sell Warrants thereunder and, when the Board of Directors of the Company has taken all necessary corporate action to authorize such Warrant Agreement and the issuance and sale of such Warrants, the Company will have the authority to execute and deliver such Warrant Agreement and to execute, issue and deliver such Warrants.

5. The Company has the corporate power to enter into a Unit Agreement and to issue and sell Units thereunder and, when the Board of Directors of the Company has taken all necessary corporate action to authorize such Unit Agreement and the issuance and sale of such Units, the Company will have the authority to execute and deliver such Unit Agreement and to execute, issue and deliver such Units.

This opinion is to be relied upon only in connection with the offer and sale of the Securities while the Registration Statement and any and all required post-effective amendments thereto are effective.

This opinion is being delivered solely for the benefit of the Company and such other persons as are entitled to rely upon it pursuant to applicable provisions of the Securities Act. Hughes, Hubbard & Reed LLP, in its capacity as counsel to the Company, may rely upon this opinion for purposes of delivering its own opinion to be filed as an exhibit to the Registration Statement with respect to the Securities. This opinion may not be used, quoted, relied upon or referred to for any other purpose, nor may this opinion be used, quoted, relied upon or referred to by any other person, for any purpose, in each case without our prior written consent.

We consent to your filing this opinion as an exhibit to the Registration Statement and to the reference to our firm in the Prospectus under the heading "Legal Matters." In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

FOLEY HOAG LLP

By: /s/ John D. Hancock
a Partner

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement Form S-3 and related Prospectus of Cycleron Therapeutics, Inc. for the registration of \$150,000,000 of debt securities, common stock, preferred stock, units and warrants, and to the incorporation by reference therein of our report dated March 12, 2020, with respect to the consolidated and combined financial statements of Cycleron Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2019, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
July 24, 2020
