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

FORM 10-K

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

For the fiscal year ended December 31, 2022

OR

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

For the transition period from _____ **to** _____

Commission file number: **001-38787**

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.)
245 First Street, 18th Floor, Cambridge, Massachusetts (Address of principal executive offices)	**02142** (Zip Code)

(857) 327-8778

Registrant's telephone number, including area code

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, no par value	**CYCN**	**The Nasdaq Capital Market LLC**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the common stock held by non-affiliates of the registrant, as of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $18.8 million, computed using the closing price on that day of $0.549.

As of March 19, 2023, there were 43,524,894 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement, to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, for its 2023 Annual Meeting of Stockholders are incorporated by reference in Part III of this Form 10-K.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by 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:

- we could be delisted from Nasdaq;
- there is substantial doubt regarding our ability to continue as a going concern;
- the timing, investment and associated activities involved in developing, obtaining regulatory approval for, launching and commercializing our product candidates, including zagociguat and CY3018;
- 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;
- the success of collaboration or license agreements of our product candidates;
- our ability to access capital, capabilities, and transactions necessary to advance the development of our assets;
- whether the praliciguat out-license will result in the creation of any therapies;
- whether any development, regulatory, and commercialization milestones or royalty payments provided for in the agreement with Akebia (as defined below) will be achieved;
- the impact on our business of 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;
- the coronavirus ("COVID-19") pandemic may continue to disrupt our business, including our development activities; and
- trends and challenges in the markets for our potential products.

You should refer to “Item 1A. Risk Factors” in this Annual Report on Form 10-K for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date following the date of this Annual Report.

You should read this report and the documents that we reference in this report, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

Unless the context requires otherwise, references in this report to “Cyclerion,” the “Company,” “we,” “us,” and “our” refer to Cyclerion Therapeutics, Inc. and, where appropriate, our consolidated subsidiaries.

PART I

Item 1. Business

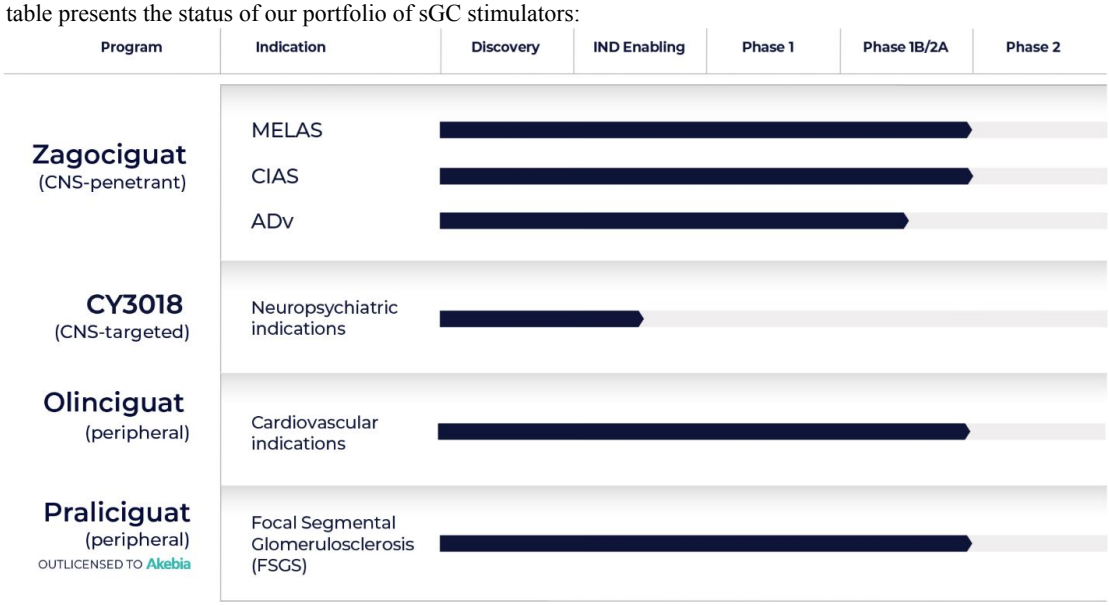
Overview

Cyclerion Therapeutics, Inc. (“Cyclerion”, the “Company” or “we”) is a biopharmaceutical company on a mission to develop treatments for serious diseases.

Cyclerion's portfolio includes novel soluble guanylate cyclase ("sGC") stimulators that modulate a key node in a fundamental signaling network in both the central nervous system ("CNS") and the periphery. The nitric oxide ("NO") soluble guanylate cyclase ("sGC") cyclic guanosine monophosphate ("cGMP") signaling pathway is a fundamental mechanism that precisely controls key aspects of physiology throughout the body. The NO-sGC-cGMP pathway regulates diverse and critical biological functions including mitochondrial function, neuronal function, inflammation, and hemodynamics. Although this pathway has been successfully targeted with several drugs in the periphery, this mechanism has yet to be fully leveraged therapeutically, particularly in the CNS, where impaired NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many neurodegenerative and neuropsychiatric diseases.

Zagociguat (previously CY6463) is a clinical-stage CNS-penetrant sGC stimulator that has shown rapid improvement in cerebral blood flow, functional brain connectivity, brain response to visual stimulus, cognitive performance, and biomarkers associated mitochondrial function and inflammation in clinical studies. CY 3018 is a CNS-targeted sGC stimulator that preferentially localizes to the brain and has a pharmacology profile that suggests its potential for the treatment of neuropsychiatric diseases and disorders. Praliciguat is a systemic sGC stimulator that is licensed to Akebia Therapeutics, Inc. ("Akebia") and being advanced in rare kidney disease. Olinciguat is a clinical-stage vascular sGC stimulator that the Company intends to out-license for cardiovascular diseases. Cyclerion is actively evaluating the best combination of capital, capabilities, and transactions available to it to advance the development of zagociguat and its other clinical development candidates and to maximize shareholder value.

The following table presents the status of our portfolio of sGC stimulators:



Cyclerion became an independent public company on April 1, 2019 after Ironwood Pharmaceuticals, Inc., or Ironwood, completed a tax-free spin-off of its sGC business, which we refer to herein as the "Separation". 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 expertise and deep experience in the NO-sGC-cGMP pathway.

Drug development involves a high degree of risk and investment, and the status, timing and scope of our development programs are subject to change. Important factors that could adversely affect our drug development efforts are discussed in the "Risk Factors" section of this Annual Report on Form 10-K.

Research and Development programs

Zagociguat is an orally administered CNS-penetrant sGC stimulator. NO-sGC-cGMP is a fundamental signaling network, including in the brain where it is critical to basic CNS functions. Deficient NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many peripheral and CNS disorders. As an sGC stimulator, zagociguat amplifies endogenous NO signaling by acting as a positive allosteric modulator to sensitize the sGC enzyme to NO and increase the production of cGMP. By compensating for deficient NO-sGC-cGMP signaling, zagociguat may have broad therapeutic potential as a treatment for people with serious diseases.

On January 13, 2020, we announced positive results from our Phase 1 first-in-human study that provided the first clinical data supporting the development of zagociguat. The results from this study indicate that zagociguat was well tolerated. Pharmacokinetic data, obtained from both blood and cerebral spinal fluid, support once-daily dosing with or without food and demonstrated zagociguat penetration of the blood-brain-barrier with concentrations in the CSF expected to be pharmacologically active.

On October 14, 2020, we announced positive topline results from our zagociguat Phase 1 translational pharmacology study in healthy elderly participants. Treatment with zagociguat for 15 days in this 24-subject study confirmed and extended results seen in the earlier first-in-human Phase 1 study: once-daily oral treatment demonstrated blood-brain-barrier penetration with expected CNS exposure and target engagement. Results also showed significant improvements in neurophysiological and objective performance measures as well as decreases in inflammatory biomarkers associated with aging and neurodegenerative diseases. Zagociguat was safe and generally well tolerated in the study. These results, together with nonclinical data, supported the continued development of zagociguat as a potential new medicine for serious diseases involving the CNS.

On June 10, 2022, we announced positive topline clinical data for zagociguat in our signal-seeking clinical study for the potential treatment of Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes ("MELAS"). In this open-label, single-arm study of the oral, once-daily sGC stimulator in eight adults aged 18 or older with MELAS, improvements were seen across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarkers such as lactate and GDF-15, a broad panel of inflammatory biomarkers, cerebral blood flow, and functional connectivity between neural networks. These positive effects after 29 days of dosing were supported by correlations among several endpoints with each other and with zagociguat plasma concentrations. Zagociguat was well tolerated with no serious or severe adverse events and no events leading to discontinuation. Pharmacokinetics were consistent with the Phase 1 studies in healthy volunteers. The positive data from this study support the potential of zagociguat to provide therapeutic benefit to people living with mitochondrial diseases, including MELAS.

On July 28, 2022, we announced positive topline data from our signal-seeking clinical study of zagociguat for the potential treatment of Cognitive Impairment Associated with Schizophrenia ("CIAS"). Data from the 14-day, double-blind, randomized, placebo-controlled, multiple-ascending-dose study in 48 adults aged 18-50 with stable schizophrenia on a stable, single, atypical antipsychotic regimen demonstrated that once-daily zagociguat was safe and well tolerated, with no reports of serious adverse events, severe adverse events, or treatment discontinuation due to adverse events. We further announced that study data demonstrated a strong effect on cognitive performance after two weeks of 15mg once-daily dosing and that positive movement on inflammatory biomarkers was also observed. These signals on exploratory endpoints are consistent with pro-cognitive and anti-inflammatory effects of zagociguat observed in preclinical studies and prior clinical trials and support the further development of oral, once-daily zagociguat.

In October 2022, the WHO International Nonproprietary Names committee and the United States Adopted Name council selected zagociguat as a nonproprietary name for CY6463.

On October 6, 2022, we announced that we had recently capped enrollment in our signal-seeking clinical study of zagociguat for the potential treatment of Alzheimer's disease with vascular pathology ("ADv"). Data from the ADv study are expected in the first half of 2023. The ADv study is supported in part by a $2 million grant from the Alzheimer's Association's Part the Cloud-Gates Partnership Grant Program (the "PTC Grant").

On March 22, 2023, we announced that given the significant capital and capabilities necessary to ensure that the MELAS Phase 2b study is executed efficiently and with the highest quality, and the currently unfavorable capital market conditions, we are actively evaluating the best combination of capital, capabilities, and transactions available to us to advance the development of zagociguat and our other clinical development candidates and to maximize shareholder value.

CY3018 is a CNS-targeted sGC stimulator in preclinical development that preferentially localizes to the brain and has a pharmacology profile that suggests its potential for the treatment of neuropsychiatric diseases and disorders.

Praliciguat is an orally administered, once-daily systemic sGC stimulator. On June 3, 2021, we entered into a license agreement with Akebia relating to the exclusive worldwide license to Akebia of our rights to the development, manufacture, medical affairs, and commercialization of pharmaceutical products containing praliciguat and other related products and forms thereof enumerated in such agreement. Cyclerion is eligible to receive up to $585 million in total potential future development, regulatory, and commercialization milestone payments. Cyclerion is also eligible to receive tiered, sales-based royalties ranging from single-digit to high-teen percentages.

Olinciguat is an orally administered, once-daily, vascular sGC stimulator that was evaluated in a Phase 2 study of participants with sickle cell disease. We released topline results from this study in October 2020. We intend to out-license olinciguat to an entity with strong cardiovascular and/or cardiopulmonary capabilities.

Our Strategy

Our mission is to develop treatments for serious diseases. The first step is identifying indications for clinical development where the scientific rationale is strong and the unmet need is high, creating a compelling opportunity. We have several product opportunities including zagociguat for mitochondrial diseases, CY3018 for neuropsychiatric diseases, and olinciguat for cardiovascular/cardiopulmonary diseases. Our focus right now is to find the best combination of capital, capabilities, and transactions that will enable the advancement of these assets for patients in a way that maximizes shareholder value.

Intellectual Property

We vigorously protect the intellectual property and proprietary technology that we believe is important to our business, including by pursuing and maintaining U.S. and foreign patents that cover our product candidates and compositions, their methods of use and the processes for their preparation, as well as any other relevant inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our commercial success depends in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions, improvements and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties.

We have twenty-six issued U.S. patents, twenty-eight pending U.S. patents applications (of which six are in the provisional stage), four pending Patent Cooperation Treaty, or PCT, application, and numerous foreign patents

and pending patent applications. The PCT applications are filed under an international patent law treaty that provides a unified procedure for filing a single initial patent application to seek patent protection for an invention simultaneously in each of the 153 contracting states, followed by the process of entering national phase, which requires a separate application in each of the member states in which national patent protection is sought.

The technology underlying our sGC patents and pending patent applications has been developed by us and was not acquired from any in-licensing agreement. We own all of the issued patents and pending applications.

The intellectual property portfolios for our most advanced product candidates are summarized below.

Zagociguat Patent Portfolio

Our patent portfolio includes four U.S. issued patents, eight pending US applications, (including three provisional cases), one PCT application, and numerous foreign patents and pending patent applications.

Two of the issued U.S. patents, US 10,858,363 and US 10,472,363 are directed to zagociguat and related compounds, and their pharmaceutical compositions thereof and will expire in 2037. The terms of these U.S. patents may be eligible for patent term extension as described below. A third U.S. patent, US 11,466,015 is directed to polymorphs of zagociguat and will expire in 2039. The fourth U.S. patent, US 11,466,014, is directed to methods of manufacturing zagociguat, and will expire in 2039. Two of the pending U.S. patent applications are directed to solid forms and processes for the large-scale synthesis of zagociguat and, if issued, will expire in 2039. Two other pending U.S. patent application are directed to compounds related to zagociguat, and, if issued, will expire in 2037 and 2041, respectively. An additional pending U.S. patent application is directed to methods of treating mitochondrial diseases with sGC stimulators including zagociguat, and, if issued, will expire in 2039. Three provisional patent applications are directed to additional methods of treatment using zagociguat.

One PCT pending application is directed to the treatment of cognition using zagociguat and if issued will expire in 2041.

Furthermore, we have one European issued patent expiring in 2037, which was validated in multiple countries, one granted patent in Japan, and eleven issued patents in other foreign jurisdictions, ten expiring in 2037, and two expiring in 2039. All of these are directed to zagociguat and related compounds, polymorphs or manufacturing processes. Some of these patents may be eligible for patent term extension depending on the jurisdiction.

CY3018 Patent Portfolio

Our CY3018 patent portfolio includes one pending U.S. provisional application, two PCT applications and several applications in foreign jurisdictions. The two PCT applications and foreign applications are directed to CY3018 and related compounds and their methods of use and if granted will expire in 2042. Some of the resulting patents, if issued, may be eligible for patent term extension or the foreign jurisdiction equivalent, depending on the jurisdiction.

Praliciguat Patent Portfolio

Our praliciguat patent portfolio includes ten U.S. issued patents, eight pending U.S. patent applications, and numerous patents and pending patent applications in foreign jurisdiction.

One of the U.S. patents, US 9,481,689, which will expire in 2034, is directed to praliciguat and pharmaceutical compositions thereof. The term of this U.S. patent may be eligible for patent term extension as described below. Two other U.S. patents, US 8,748,442 and US 9,139,564, expire in 2031, and provide generic coverage of praliciguat and intermediates used in the preparation of praliciguat, respectively. A fourth U.S. patent, US 10,183,021 will expire in 2034 and is directed to the treatment of resistant hypertension with praliciguat or combinations of praliciguat and known anti-hypertensives. A fifth U.S. patent, US 209,639,308 will expire in 2034

and is directed to the treatment of diabetic nephropathy with praliciguat or combinations of praliciguat with other agents. The sixth U.S. patent, US 10,927,136 covers phosphorus prodrugs of praliciguat and will expire in 2037. The seventh U.S. Patent, US 11,389,449, is directed to the treatment of metabolic syndrome with praliciguat and will expire in 2038. The eighth U.S. Patent, US 11,357,777, is directed to the treatment of NASH with praliciguat and other compounds and will expire in 2037. The ninth and tenth U.S. Patents, US 11,319,308 and 11,274,096, are directed to the syntheses of intermediates useful in the manufacture of praliciguat.

Two pending U.S. patent applications that, if issued, will expire in 2031 and 2034, respectively, provide generic coverage for praliciguat. Two additional U.S. patent applications that, if issued, will expire in 2037, and 2039, respectively, provide coverage for methods of large scale preparation of praliciguat. We also have a pending U.S. application directed to a praliciguat formulation, that, if issued, will expire in 2036.

Another of the U.S. pending applications is directed to methods of treating diabetic nephropathy with praliciguat, that if issued, will expire in 2040 or later. The remaining two pending U.S. applications are directed to prodrugs of praliciguat, and deuterated forms of praliciguat and, if issued, will expire in 2037 and 2040, respectively.

Furthermore, we have four granted European patents, one expiring in 2031, another one in 2032, a third one in 2034, and a fourth one in 2037, each of them validated in multiple countries; five granted Japanese patents, one expiring in 2031, another in 2034, one in 2036 and two others in 2037; six granted Chinese patents, two expiring in 2031, one in 2032, two in 2034, and one expiring in 2037; and thirty-nine issued patents in other foreign jurisdictions, two expiring in 2032, twelve of them expiring in 2031, nine expiring in 2034, three expiring in 2036, and thirteen in 2037. Some of these patents may be eligible for patent term extension depending on the jurisdiction. We also have numerous patent applications pending in foreign jurisdictions.

Olinciguat Patent Portfolio

Our olinciguat patent portfolio includes nine U.S. issued patents, five pending U.S. patent applications, one PCT patent application and numerous patents and pending applications in foreign jurisdictions.

One of the U.S. patents, US 9,586,937, which will expire in 2034, is directed to olinciguat and pharmaceutical compositions thereof. The term of this U.S. patent may be eligible for patent term extension as described below. Two other U.S. patents, US 8,748,442 and US 9,139,564, expire in 2031, and provide generic coverage of olinciguat and intermediates used in the preparation of olinciguat, respectively. Another U.S. patent, US 10,517,874, which will expire in 2034 is directed to the treatment of SCD using olinciguat alone or in combinations with other therapeutic agents. A fifth U.S. issued patent, US 10,889,577, will expire in 2037 and is directed to polymorphs of olinciguat. The sixth issued patent, US 11,207,323, will expire in 2034 and provides coverage for stereoisomers of olinciguat. Two U.S. issued patents, US 11,319,308 and 11,274,096, are directed to the syntheses of intermediates useful in the manufacture of olinciguat and will expire in 2037 and 2039, respectively. The ninth U.S. Patent, US 11,357,777, is directed to the treatment of NASH with olinciguat and other compounds and will expire in 2037.

Two pending U.S. patent applications, if issued, will expired in 2037 and provide additional coverage for polymorphs of olinciguat. Another pending U.S. patent application, if issued, will expire in 2031, and provides generic coverage for olinciguat. The remaining pending U.S. patent applications are directed to deuterated forms of olinciguat and processes and synthetic intermediates for preparing olinciguat and, if issued, will expire in 2040 and 2037, respectively.

The PCT patent application is directed to the treatment of heart failure with preserved ejection fraction (HFpEF) in post-menopausal women with olinciguat and other sGC stimulators. If issued, the corresponding patents will expire in 2042.

Furthermore, we have four granted European patents, one expiring in 2031, another in 2032, a third one in 2034, and a fourth one in 2037, each of them validated in multiple countries; seven granted Japanese patents, one expiring in 2031, three others in 2034, and three expiring in 2037; five granted Chinese patents, two expiring in

2031, another one in 2032, and two more in 2034; and forty issued patents in other foreign jurisdictions, twelve of them expiring in 2031, two expiring in 2032, ten expiring in 2034, and sixteen expiring in 2037. We also have numerous pending patent applications in foreign jurisdictions. Some of these patents may be eligible for patent term extension or the foreign jurisdiction equivalent, depending on the jurisdiction.

Additional Intellectual Property

In addition to the patents and patent applications related to zagociguat, CY3018, praliciguat, and olinciguat, we currently have seven issued U.S. patents; eight patents granted in foreign jurisdictions, including European patents that have each been validated in several countries; and a number of pending U.S. (including provisional applications) and foreign pending patent applications directed to other sGC stimulator molecules and uses thereof.

Patent Term

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application, assuming that all applicable maintenance or annuity fees are paid. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in that country, and the validity and enforceability of the patent.

In addition, the term of a U.S. patent that covers an FDA-approved drug may be eligible for patent term extension under the Drug Price Competition and Hatch-Waxman Act, to account for some of the time the drug is under development and regulatory review after the patent is granted. For a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug (drug substance or drug product), an FDA-approved method of treatment using the drug and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have similar patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency.

Trade Secrets and Proprietary Information

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We typically 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. We protect our proprietary information, including trade secrets and know-how, by establishing confidentiality agreements with our commercial partners, collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees, consultants, scientific advisors and contractors. These agreements generally provide that all confidential information developed or made known during the course of an individual or entities' relationship with us must be kept confidential during and after the relationship. These agreements also typically provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. However, these agreements may be breached, and we may not have adequate remedies for any breach. We also take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual

property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation

United States Regulation

The FDA regulates medical products, including prescription drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations. Products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including imposition of a clinical hold, refusal by the FDA to approve applications, withdrawal of an approval, import/export delays, issuance of warning letters and other types of enforcement letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, debarment, or civil or criminal investigations and penalties brought by the FDA, the Department of Justice, State Attorneys General, or other governmental entities.

The process required by the FDA before a drug may be approved and marketed in the United States generally involves the following:

- completion of extensive nonclinical laboratory and animal studies conducted in accordance with applicable regulations, including Good Laboratory Practices, or GLP, regulations and applicable requirements for the humane use of laboratory animals;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may commence;
- approval by an independent IRB to proceed with initiating the clinical trial at each corresponding investigational site.
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, GCPs and other clinical-trial related regulations to establish the safety and efficacy of the product for each proposed indication;
- preparation and submission to the FDA of an NDA;
- satisfactory completion of one or more FDA inspections such as pre-approval inspection(s) of the manufacturing facility or facilities at which the product, or components thereof, are made to assess compliance with current GMP;
- payment of user fees for FDA review of the NDA; and
- FDA acceptance, review and approval of the NDA, which may include an Advisory Committee review.

The development and approval process requires substantial time, effort and financial resources and the receipt and timing of any approval is uncertain.

Nonclinical and Clinical Trials in Support of an NDA

Before testing any drug product candidate in humans, the product candidate must undergo rigorous nonclinical testing. Nonclinical studies include laboratory evaluations of the product candidate, as well as in vitro and animal studies to assess the potential safety and efficacy of the product candidate. The conduct of nonclinical studies that determine the product safety information for administration to humans must comply with federal regulations and requirements, including GLP regulations. The sponsor must submit the results of the nonclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical study protocol, to the FDA as part of an IND, which must become effective before clinical trials in

a given indication may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the content of the IND or the conduct of the proposed trial(s) as outlined in the IND prior to that time. In such a case, the IND sponsor must resolve any outstanding concerns with the FDA before the clinical trial(s) can proceed.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCP requirements. Each clinical trial must be reviewed and approved by an IRB for the sites at which the trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. The IRB also approves the informed consent form, including a privacy statement, that must be provided to each clinical trial participant or his or her legal representative, and must monitor the clinical trial until completed.

Clinical trials are typically conducted in three sequential phases prior to approval, which may overlap or be combined:

- *Phase 1.* Phase 1 clinical trials generally involve a small number of healthy participants or disease-affected participants who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacokinetics, pharmacologic action, side effect tolerability and safety of the drug.
- *Phase 2.* Phase 2 clinical trials usually involve studies in a limited population of participants with a disease or disorder to evaluate the efficacy of the product candidate for specific indications, determine dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.
- *Phase 3.* Phase 3 clinical trials generally involve a larger number of participants at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, to establish the overall benefit/risk profile of the product and to provide an adequate basis for product approval by the FDA.
- *Phase 4.* Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be required to be conducted after approval to gain additional experience from the treatment of participants in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA. Failure to conduct the Phase 4 clinical trials per the plan required by the FDA could result in enforcement action or withdrawal of approval.

Progress reports detailing new information and changes such as the results of clinical trials, new nonclinical studies, new product quality data, or changes to manufacturing controls must be submitted at least annually to the FDA and more frequently if serious adverse events occur. The FDA or the sponsor may suspend or terminate a clinical trial at any time, or the FDA may impose other sanctions on various grounds, including a finding that the research participants are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the requirements of the IRB or if the drug has been associated with unexpected serious harm to participants. There are also requirements related to registration and reporting of certain clinical trials and completed clinical trial results to public registries.

Submission and Review of an NDA

Assuming successful completion of the required nonclinical and clinical testing, the results of nonclinical studies and clinical trials, together with detailed information on the product's manufacture, composition, quality controls and proposed labeling, among other things, are submitted to the FDA in the form of an NDA, requesting approval to market the product for one or more indications. The application must be accompanied by a significant user fee payment, which typically increases annually, although waivers may be granted in limited cases (e.g., for products that have received an Orphan Designation).

The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and may require additional nonclinical or clinical studies, or other information (e.g., product quality data or manufacturing controls) before it accepts the filing. If an NDA has been accepted for filing, which occurs 60 days after submission, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original NDAs, the FDA has ten months from the filing date in which to complete its review of a standard application, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process may be significantly extended by FDA requests for additional information and clinical data or clarification.

The FDA reviews NDAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with current GMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA typically will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facilities comply with current GMP. Additionally, the FDA will frequently inspect one or more clinical trial sites for compliance with GCPs and integrity of the data supporting safety and efficacy.

During the approval process, the FDA will also prepare an integrated benefit-risk assessment and determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to ensure that the benefits of the drug outweigh the risks and to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS. A REMS that includes elements to assure safe use, or ETASU, can substantially increase the costs of commercializing a drug. The FDA could also require a special warning, known as a boxed warning, to be included in the product label in order to highlight a particular safety risk. Boxed warnings may limit the type of advertising for a drug. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, FDA will issue either an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug and is accompanied by specific prescribing information for specific conditions of use. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the submission identified by the FDA and may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either amend the NDA with data to address the raised concerns, resubmit the NDA addressing all the deficiencies identified in the letter, engage in dispute resolution with the FDA about the identified deficiencies in the CRL, or withdraw the application. Even with submission of this additional information, the FDA may ultimately decide that the re-submitted application does not satisfy the regulatory criteria for approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States, or in other limited cases. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process, though companies developing orphan drugs may be eligible for certain incentives, including tax credits for qualified clinical testing.

Generally, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same active moiety for the same indication for seven years from the date of such approval, except in limited circumstances. Competitors, however, may receive approval of different active moieties for the same indication or obtain approval for the same active moiety for a different indication. If one of our product candidates designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity.

Expedited Review and Approval

The FDA has various programs that are intended to expedite development and approval of drugs intended for the treatment of serious or life-threatening diseases or conditions and that demonstrate the potential to address unmet medical needs.

An application may be eligible for a "fast track" designation for a product that is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. Fast track designation provides opportunities for more frequent interactions with the FDA review team and permits FDA to consider sections of the NDA on a rolling basis before the complete application is submitted.

In addition, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor.

An application may be eligible for "accelerated approval" where the product candidate is intended to treat a serious or life-threatening illness and provides meaningful therapeutic benefit over existing treatments; applications eligible for accelerated approval may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA requires a sponsor to conduct confirmatory studies to verify the predicted effect on IMM or another clinical endpoint, and the product may be subject to expedited withdrawal procedures.

Once an NDA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if the FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. Under priority review, the FDA must review an application in six months, compared to ten months for a standard review. A product may be eligible for more than one expedited approval program. Even if a product qualifies for one or more of these programs, however, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, these expedited review pathways do not change the standards for approval and may not ultimately expedite the development or approval process.

Non-Patent Exclusivity

In addition to patent exclusivity, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA for approval of a generic or 505(b)(2) application that relies on the listed drug as protected by regulatory exclusivity.

An NDA for a new chemical entity may receive five years of exclusivity, whereby the FDA will not accept for filing, with limited exceptions, a product seeking to rely upon the FDA's findings of safety or effectiveness for such new chemical entity. An ANDA containing a paragraph IV patent certification can be filed after four years. Alternatively, an NDA may obtain a three-year period of non-patent market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing

regulatory exclusivity for both drugs and biologics, and also unexpired Orange Book listed patents in the case of drugs. This six-month exclusivity may be granted if a sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims and some manufacturing and supplier changes, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for marketed products and the establishments where such products are manufactured, as well as new application fees for certain supplemental applications. The FDA may impose a number of post-approval requirements as a condition of approval of an NDA, such as Phase 4 clinical trials or a REMS.

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

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Corrective action could delay product distribution and require significant time and financial expenditures. Later discovery of previously unknown safety issues with a product, including adverse events of unanticipated severity or frequency, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters of clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications, in accordance with the provisions of the approved label and FDA guidance. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Additionally, all promotional material must be truthful and non-misleading, and present balanced information regarding the risks and benefits of the drug product.

Other Regulatory Requirements

Outside the U.S., our abilities to develop and market a product are contingent upon receiving approval and ultimately marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from jurisdiction to jurisdiction. At present, foreign marketing authorizations are applied for at a national level, although within the E.U. registration procedures are available to companies wishing to market a product in more than one E.U. member state.

We are subject to U.S. federal and foreign anti-corruption laws. Those laws include the U.S. Foreign Corrupt Practices Act, or 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 encompasses certain healthcare professionals in many countries. We are also subject to similar laws of other countries that have enacted anti-corruption laws and regulations.

Pediatric Development

In the European Union, companies developing a new medicinal product must agree to a Pediatric Investigation Plan, or PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a deferral or waiver applies, (e.g., because the relevant disease or condition occurs only in adults). The MAA for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Where the MAA includes the results of all pediatric studies conducted in accordance with the PIP and the results are reflected in the approved summary of product characteristics, the holder of a patent or supplementary protection certificate is entitled to receive a six-month extension of the protection under a supplementary protection certificate or, in the case of orphan medicinal products, the product is eligible for a two-year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

In the US, under Pediatric Research Equity Act (PREA), a pediatric development plan is required to accompany an NDA for all drugs, except those receiving non-oncology Orphan Drug Designation. This may include waiver or deferral of pediatric studies. The Best Pharmaceuticals for Children Act (BPCA) also allows for agreement with FDA on a pediatric written request that, if fulfilled, may extend data exclusivity for the molecule for an additional 6 months.

Competition

The biopharmaceutical industry is highly competitive within and across therapeutic categories and indications. There are many public and private biopharmaceutical companies, universities, government agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. In addition, the number of companies seeking to develop and commercialize products and therapies competing with our product candidates is likely to increase. However, we seek to build our portfolio with key differentiating attributes to provide a competitive advantage in the markets we target. The success of all of our product candidates, if approved, will likely depend upon their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Many of our competitors, including those mentioned below, may have greater financial resources and broader expertise in research and development, manufacturing, nonclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved medicines than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with Cyclerion in establishing clinical trial sites and participant registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Competition can be viewed as through at least two lenses: 1) companies that are developing products with a different mechanism of action to address the same therapeutic need and 2) companies that are developing products that act through the same mechanism of action (i.e., sGC modulators).

Competition within target therapeutic areas.

We believe Biogen, Sage, Otsuka, Neumora, Tonix, Neurocrine, Pfizer, atai Life Sciences, Alto Neuroscience, Cerevel, Karuna, PTC Therapeutics, Khondrion B.V, Abliva AB, Reneo, Travere Therapeutics, Dimerix Limited, Vertex Pharmaceuticals, Chinook Therapeutics, Boehringer Ingelheim, Acelyrin, River 3 Renal Corp, Astellas, Pfizer, Eli Lilly, Novartis, AstraZeneca, Bayer and Merck are our most direct competitors with respect to zagociguat, CY3018, praliciguat, and olinciguat.

Competition within the sGC mechanism.

There is one major competitor that is actively developing sGC modulators. Bayer and Merck have an active collaboration on sGC stimulators, focused primarily on cardiovascular, pulmonary, and renal indications. They have two approved sGC stimulators, ADEMPAS® (riociguat), indicated for PAH and CTEPH, and VERQUVO® (vericiguat) for heart failure with reduced ejection fraction (HFrEF). We are not aware of any efforts to develop sGC modulators for treatment of CNS diseases.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We depend on third-party contract manufacturing organizations, or CMOs, for all our requirements of raw materials, drug substance and drug product for our ongoing clinical trials and our nonclinical research. We intend to continue to rely on CMOs for the supply of zagociguat and CY3018 for all stages of clinical development and commercialization, as well as for the supply of any other product candidates that we may identify. We require all our CMOs to conduct manufacturing activities in compliance with current GMP requirements.

We believe that zagociguat and CY3018 drug substance and drug product may be manufactured from readily available raw materials and the processes are amenable to large-scale production and do not require unusual equipment or handling. We believe adequate supply of zagociguat and CY3018 drug substance and drug product is readily available from our current CMOs to satisfy our immediate clinical and nonclinical demands. We obtain our supplies from these CMOs on a purchase order basis and do not have arrangements in place for long-term supply or redundant supply of zagociguat and CY3018; however, we are working with our CMOs to implement improvements to our drug substance and drug product manufacturing processes to further ensure product capacity adequate to meet further development demands. We are evaluating CMOs for drug substance and drug product that could meet potential commercial demands.

Human Capital Resources

We have an exceptional and diverse team of individuals who have a passion for developing important new medicines that will have a profound impact on the lives of patients with serious CNS diseases. As a small, innovative company, our success depends on attracting, retaining and motivating highly skilled and experienced scientific, medical and other personnel. Our ability to recruit and retain such employees depends on a number of factors, including our distinct corporate culture, and our collaborative work environment. We provide robust compensation and benefits programs which include competitive salaries, potential annual discretionary bonuses, stock awards, a 401(k) plan with employer match, healthcare and insurance benefits, health savings and flexible spending accounts, unlimited vacation time, among other benefits. Our employees are further guided by our code of conduct and our cultural values of seeking to serve patients, acting with integrity, empowering people and innovating for solutions.

We are committed to our employees' health, safety and wellness. We provide our employees and their families with access to a variety of innovative, flexible and convenient health and wellness programs. In response to the COVID-19 pandemic, we implemented significant changes that were determined to be in the best interest of our

employees and the communities in which we live and work, while continuing to ensure the safety of patients in our trials.

Employee Profile

As of December 31, 2022, we had sixteen (16) employees, of which eight (8) employees hold Ph.D. or Pharm.D. degrees. Of the sixteen (16) employees, eight (8) are in our development organization, two (2) are in our strategy and corporate development organizations and six (6) are in general and administrative functions. None of our employees are subject to a collective bargaining agreement or represented by a trade or labor union. We consider our employee relations to be good.

During the year ended December 31, 2022, we initiated certain reductions in our workforce. Refer to Note 12, *Workforce Reduction,* to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further details.

Corporate Information

We were incorporated in the Commonwealth of Massachusetts on September 6, 2018. Our principal executive offices are located at 245 First Street, Riverview II, 18th Floor, Cambridge, MA 02142. Our telephone number is (857) 327-8778. Our common stock is listed on the Nasdaq Capital Market under the symbol "CYCN."

Available Information

Our internet website address is www.cyclerion.com. In addition to the information contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or the SEC. The SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

Item 1A. Risk Factors.

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 Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. 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. In this section, we first provide a summary of the more significant risks and uncertainties we face and then provide a full set of risk factors and discuss them in greater detail.

Risk Factors Summary

- We are a biopharmaceutical company with a limited operating history and no products approved for commercial sale.
- We have incurred significant losses and have never generated revenue from product sales; we anticipate that we will continue to incur significant losses for the foreseeable future and may never be profitable.
- There is substantial doubt regarding our ability to continue as a going concern. We will need to raise additional funding, which may not be available on acceptable terms, if at all to continue as a going

concern and advance our product candidates. 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.

- Our approach to the discovery and development of our product candidates may never lead to marketable products.
- We may encounter substantial delays in our activities, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities in the development of our compounds.
- The COVID-19 pandemic may continue to disrupt our business, including our development activities.
- We could encounter difficulties in enrolling participants in our clinical studies, which could delay or prevent progress of our product candidates.
- We may be unable to obtain regulatory approval for our product candidates and unable to generate product revenue.
- Our product candidates may cause side effects that may result in label restrictions.
- We may have to change our nonclinical or clinical study protocols due to regulatory reasons or unanticipated events, which could result in increased costs to us and could delay our development timeline.
- We may not succeed in our pursuit of capital, capabilities, and transactions for the development and commercialization of our assets.
- Akebia may not be successful in developing any therapies through the praliciguat out-license with the Company.
- We may enter into collaboration or license arrangements in the future that ultimately are not successful.
- We rely, and expect that we will continue to rely, on third parties to conduct nonclinical and clinical studies and to manufacture drug supplies for our product candidates. If these third parties do not execute successfully, our business could be substantially harmed.
- We share confidential information with third-party vendors, including trade secrets and know-how, which increases the possibility that our confidential information will be misappropriated or disclosed.
- We may be unable to adequately protect our proprietary technologies or obtain and maintain issued patents that are sufficient to protect our product candidates.
- We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts.
- We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.
- 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.
- We may not be able to obtain additional protection under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates.
- 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.
- If the market opportunities for our product candidates are smaller than we estimate, our revenue and ability to achieve profitability may be harmed.
- We may fail to comply with healthcare and other regulations and could face substantial penalties.

- Our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours.
- The impact of healthcare reform and other governmental and private payor initiatives may harm our business.
- Our prospects for success depend on our ability to retain our management team and to attract, retain and motivate qualified personnel.
- We may need to expand our organization and we may experience difficulties in managing growth of our employee base.
- We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.
- We could fail to maintain proper and effective internal controls and our ability to produce accurate and timely financial statements could be impaired.
- 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.
- 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.
- We could be adversely affected by violations of the U.S. Foreign Corrupt Practices Act, or the FCPA, and other worldwide anti-bribery laws.
- Our failure to regain compliance with Nasdaq's continued listing requirements, could result in the delisting of our common stock.
- We have limited trading history and a relatively low-volume trading market for our shares and our common stock market price may fluctuate widely.
- 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.

Risks Related to Our Financial Position and Capital Needs

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

We are a 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 product candidates.

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, 2022 and 2021 were $44.1 million and $51.6 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 product candidates.

Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency (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.

There is substantial doubt about our ability to continue as a going concern. We will need to raise additional funding, which may not be available on acceptable terms, if at all to continue as a going concern and advance our product candidates. 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.

There is substantial doubt regarding our ability to continue as a going concern. As of December 31, 2022, we had unrestricted cash and cash equivalents of approximately $13.4 million. Our management believes that such cash and cash equivalents will not be sufficient to fund our operating expenses and capital requirements for one year after the date the financial statements are issued, whether or not we curtail efforts with respect to certain of our product candidates. We will require significant additional funding to advance any of our product candidates beyond the short-term and to sustain our operations.

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 product 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 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.

Risks Related to our Business and Industry

Our approach to the discovery and development of product candidates for the treatment of serious CNS diseases may never lead to marketable products.

We are focusing our research and development efforts on addressing serious CNS diseases. The development of CNS therapies presents unique challenges, including an imperfect understanding of the biology, the presence of the blood-brain barrier that can restrict the flow of drugs to the brain, a frequent lack of translatability of

nonclinical study results in subsequent clinical trials and dose selection, and the product candidate having an effect that may be too small to be detected using the outcome measures selected in clinical trials or if the outcomes measured do not reach statistical significance. Our future success is highly dependent on the successful development of our technology and our product candidates for treating CNS. 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, we will not become profitable and the value of our common stock may decline.

Research and development of biopharmaceutical products is inherently risky. We may encounter substantial delays in our activities, including our clinical studies, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities in the development of zagociguat and CY3018 to treat patients with serious diseases.

Our business depends heavily on the successful development, clinical testing, regulatory approvals and commercialization of our product candidates. Any of our current or potential product candidates, will require regulatory approvals based on 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 nonclinical 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 nonclinical testing and early clinical studies. Companies in the biopharmaceutical industry often suffer significant setbacks in later-stage clinical studies; most product candidates that begin clinical studies are never approved for commercialization by regulatory authorities. Favorable results in earlier stage trials may not be replicated in later stage trials. If we fail to produce positive results in our clinical trials, the development timeline, regulatory approval and commercialization prospects of our assets and, correspondingly, our business and financial prospects, would be materially adversely affected.

The COVID-19 pandemic continues to disrupt our business, including our development activities.

Many nations, including the United States, continue to implement mitigation measures, that have limited and may continue to limit our ability to access patients and physicians at certain local clinical centers that are participating in our development activities.

We may continue to face limitations and difficulties enrolling patients in our planned and future clinical trials if the patient populations that are eligible for our clinical trials continue to be affected by the coronavirus and/or the COVID-19 vaccines. COVID-19 restrictions and/or COVID-19 vaccination efforts at trial sites could delay our clinical studies. In addition, if the patients enrolled in our clinical trials become infected with COVID-19, we may have more adverse events and deaths in our clinical trials as a result. Vulnerable patients, including patients with serious diseases of the CNS, such as the patients enrolling in our clinical trials, may be at a higher risk of contracting COVID-19 and may experience more severe symptoms from the disease, adversely affecting our chances for regulatory approval or requiring further clinical studies. The adverse effects that may occur from administration of COVID-19 vaccines to patients participating in our clinical trials may adversely affect our clinical trial outcomes or data analysis. Furthermore, the extent to which the pandemic, or future outbreaks of infectious disease, hinders access to facilities, procurement of resources, raw materials or components necessary for research studies or preclinical or clinical development is not fully predictable. Delays and disruptions from the pandemic, or future outbreaks of infectious disease, may increase our capital needs while potentially interfering with our access to capital.

In the event of difficulties in enrolling participants in any clinical studies conducted on our product candidates, those clinical trials could be delayed or prevented from proceeding.

Identifying and qualifying participants to participate in any clinical studies of our product candidates would be critical to the success of those clinical trials. The timing of any clinical studies will depend in part on the speed at which participants can be recruited to participate in testing our product candidates. Estimates of the prevalence of target indications may vary considerably. Determining the incidence of these conditions, including in specific geographies or demographic groups, would be challenging. The lower the actual prevalence of these conditions, the more challenges would be encountered enrolling participants in those clinical studies, which could delay development of those 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, the 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 sufficient participants cannot be enrolled in clinical studies in a timely way, obtaining study results would 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 or our licensees, as applicable, 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.

A product candidate cannot be commercialized 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 data are insufficient for approval and require additional nonclinical, clinical, or other information (e.g., product quality data or manufacturing controls). No regulatory approval for any of our product candidates has been requested or obtained, and it is possible that none of our existing product candidates or any product candidates we or our licensees may seek to develop in the future will ever obtain regulatory approval.

Any ongoing clinical studies may not be completed on schedule, and any 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 ongoing clinical studies be suspended through imposition of clinical holds;
- negative results from 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(s) to conduct a clinical study at a prospective site or sites;
- challenges in recruiting and enrolling participants 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 nonclinical and clinical assessment;
- we or our licensees may decide, or regulatory authorities may require the conduct of additional clinical studies or abandonment of 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 a clinical study's design and the interpretation of data from clinical studies, or may change the requirements for approval even after it has reviewed and commented on the design for clinical studies;
- reports from nonclinical 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, our licensees, the FDA or other comparable authorities, the IRBs or ECs overseeing a clinical study, a data and safety monitoring board overseeing the clinical study, 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 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 undertaking corrective action, including in response to the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in 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 or adverse events that are presented in the product labeling approved by regulatory authorities. Some may result in label restrictions.

As with ADEMPAS® (riociguat), and VERQUVO® (vericiguat), the only FDA-approved sGC stimulators to date, our product candidates may cause serious birth defects or miscarriage if taken while pregnant, and clinical studies for these product candidates require stringent contraceptive safeguards to prevent pregnancy. Additionally, undesirable side effects that may be observed with our product candidates could cause us, our licensees, 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 nonclinical studies and clinical studies of our product candidates may occur, which may result in changes to nonclinical or clinical study protocols or additional nonclinical or clinical study requirements, which could result in increased costs and could delay development timelines.

Changes in regulatory requirements, FDA guidance or unanticipated events during nonclinical studies and clinical studies may force amendment to nonclinical studies and clinical study protocols or the FDA may impose additional nonclinical studies and clinical study requirements. Amendments or changes to 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 nonclinical studies may increase the cost or delay the timing or successful completion of those nonclinical studies. In the event of delays in completing, or the termination of, any of nonclinical or clinical studies, or if it is required that additional nonclinical or clinical studies be conducted, the commercial prospects for 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 there will be success in obtaining regulatory approval of our product candidates in other jurisdictions.

In order to market any product outside of the United States, compliance with the numerous and varying safety, efficacy and other regulatory requirements of other countries is required. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that obtaining or maintaining regulatory approval in any other jurisdiction will be possible, 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 nonclinical 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 intended to be charged for a product candidate is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs and could delay or prevent the introduction of our product candidates in certain countries. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair the ability to market product candidates in such countries. Any such impairment would reduce the size of the 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 or our licensees may seek to secure for our product candidates. Many of these have risk of loss of exclusivity if the competitive landscape changes or regulations are revised. If we seek and are awarded orphan drug designation in the US and/or 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 our 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 capital, capabilities, and transactions for the development and commercialization of zagociguat and our other clinical stage assets, which would affect our financial condition.

We are seeking capital, capabilities, and transactions to advance the development of zagociguat and our other clinical stage assets. There can be no assurance that this process will result in any effective negotiations toward, reaching terms of, executing agreements relating to, or completing any transaction or that any such

transaction will be successful. Failure to complete any of the foregoing efforts would materially adversely affect our business, prospects, financial condition and results of operations.

Akebia may not be successful in developing any therapies through the praliciguat out-license and we may not realize any future revenue from the out-license.

On June 3, 2021, we entered into a license agreement with Akebia relating to the exclusive worldwide license to Akebia of our rights to the development, manufacture, medical affairs and commercialization of pharmaceutical products containing the pharmaceutical compound praliciguat and other related products and forms thereof enumerated in such agreement. Under the agreement, Akebia is responsible for all research, development, regulatory, and commercialization activities for certain products. Cyclerion is eligible to receive up to $12 million upon the initiation of a phase 2 clinical trial. Further milestone cash payments by Akebia are scheduled in the Agreement based on the initiation of phase 3 clinical trials in the U.S. for such products for first and second indication, for FDA approvals, for approvals in certain other major markets, and for certain sales milestones. In addition to these cash milestone payments, Akebia will pay Cyclerion tiered royalty payments on net sales in certain major markets at percentages ranging from the mid-single digits to the high-teens, subject to certain reductions and offsets. The agreement may be terminated by either party in the event a material breach by the other party, by us in the event of certain patent disputes or the failure by Akebia to initiate phase 2 clinical trials within a set period of time, and by Akebia, subject to a notice period, at any time after one year from the effective date. There can be no assurances that the agreement will result in any therapies or that it will not be terminated prior to the realization by us of any remaining eligible revenues.

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 may seek additional 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 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 nonclinical or clinical studies for our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, necessary regulatory approvals for or commercialization of our product candidates may not be obtainable and our business could be substantially harmed.

We do not have the infrastructure or internal resources and capabilities to independently conduct nonclinical or clinical studies. We rely on contract laboratories, medical institutions, clinical investigators, licensees and other third parties, such as CROs, to conduct nonclinical studies on our discovery compounds and product candidates and clinical studies on product candidates. We rely heavily on such parties for execution of nonclinical and clinical studies and can control only certain aspects of their activities. As a result, we have limited direct control over the conduct, timing and completion of our nonclinical and clinical studies and the management of data developed through these studies. 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 nonclinical and clinical studies and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we may be responsible for ensuring that each of our nonclinical and clinical studies is conducted in accordance with any applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs and other third parties does not necessarily relieve us of our regulatory responsibilities. We, our CROs and other third parties are required to comply with regulations and guidelines, such as good laboratory practices (GLPs), good clinical practices (GCPs), and current Good Manufacturing Practices. These regulations are enforced by the FDA and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces compliance to regulations through periodic inspections of clinical study sponsors, principal investigators, and third parties. If the FDA determines there was a failure to comply with the regulations the clinical data generated in any clinical studies may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require the performance of additional clinical studies before approving any marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our nonclinical studies, clinical studies or product manufacturing complies with these regulations. Our failure or the failure of our CROs or other third parties to comply with these regulations may require the repeat of those clinical studies, which would delay the regulatory approval process and could also result in enforcement action up to and including civil and criminal penalties.

Although we or our licensees may design or approve the designs of our product candidate clinical studies, CROs and other third parties conduct those clinical studies. As a result, many important aspects of the execution of the development programs for our product candidates may be outside of our direct control. In addition, the CROs, or other third parties, may not perform all of their obligations under arrangements with us or our licensees or in compliance with regulatory requirements, but we may 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 clinical studies. If the CROs, or our licensees, 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 not be able to control the amount and timing of resources these CROs or our licensees devote to our clinical products.

If any relationships with these third-party CROs terminate, arrangements with alternative CROs, may not be achievable. 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 required clinical protocols, regulatory requirements or for other reasons, any clinical studies such CROs are associated with may be extended, delayed or terminated, and required regulatory approval for or successfully commercialization of our product candidates may not be obtainable. 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, or lost.

Except as out-licensed, we must rely completely on third-party suppliers to manufacture any nonclinical 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 drug supply of our product candidates, or any future product candidates, for use in the conduct of our nonclinical and clinical studies. We lack the internal resources and the capability to manufacture any product candidates on any scale. We depend on third-party contract manufacturing organizations, or CMOs, for all our requirements of raw materials, drug substance and drug product for our future and/or ongoing nonclinical studies and clinical trials. 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 later-stage development and commercialization, as well as for the supply of any other discovery compounds or 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 nonclinical and 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 and other third parties to conduct our nonclinical studies and 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 or our licensees are unable to adequately protect proprietary technologies, 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 and our licensees 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 patents, should they issue, preserve the confidentiality of 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 product candidates and compositions, their methods of use and any other inventions that are important to the development of our business.

We have twenty-six issued U.S. patents, twenty-eight pending U.S. patents applications (of which six are in the provisional stage), four pending Patent Cooperation Treaty, or PCT, applications, and numerous foreign patents and pending patent applications. The PCT applications are filed under an international patent law treaty that provides a unified procedure for filing a single initial patent application to seek patent protection for an invention simultaneously in each of the 153 contracting states, followed by the process of entering national phase, which requires a separate application in each of the member states in which national patent protection is sought.

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. 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 patent applications are issued, competitors and other third parties may infringe, misappropriate or otherwise violate patents and other intellectual property rights. We may not be able to prevent infringement, misappropriation or other violations of 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, filing infringement claims may be required, which can be expensive and time-consuming and divert the attention of management and key personnel from business operations.

Moreover, 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 or our licensees may be necessary to determine the priority of inventions with respect to patents or patent applications. An unfavorable outcome could require ceasing the use of 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 a license on commercially reasonable terms. Involvement in litigation or interference proceedings may fail and, even if successful, may result in substantial costs, and distract management and other employees. Furthermore, an adverse decision in an interference or derivation proceeding can result in a third party receiving the sought-out patent right, which in turn could affect the 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 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, 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 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 patent rights, even if successful, would be costly and time-consuming and would divert the attention of management and key personnel from 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 any patents, if and when issued, put those patents at risk of being invalidated, held unenforceable or not infringed, or interpreted narrowly. Such proceedings could also provoke third parties to assert counterclaims, including that some or all of the claims in one or more 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, or the USPTO, or made a misleading statement, during prosecution of the patent application. In an infringement proceeding, a court may disagree with allegations and refuse to stop the other party from using the technology at issue on the grounds that patents do not cover the technology in question or may decide that a patent is invalid or unenforceable. An adverse result in any litigation, defense or post-grant proceedings could result in one or more 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 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, there cannot be certainty that there is no invalidating prior art, of which we, our licensees and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, at least part, and perhaps all, of the patent protection on our product candidates could be lost.

If any 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 product candidates. 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, non-academic outside scientific collaborators 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 parties rendering services whenever possible. However, we may not be able to enter into these agreements with all parties (for example with academic collaborators) 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, or we may have to in-license intellectual property owned by another party. 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 patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies and 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 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 and our licensees 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 are believed to provide coverage for our product candidates, we, and our licensees, 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 it is unlikely to pursue and maintain patents in all countries worldwide. As such, competitors may use technologies in jurisdictions where patent protection is not pursued and obtained 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, it may not be possible to prevent third parties from practicing our inventions in all countries outside the United States even if there is a patent in that jurisdiction. Further, a competitor may export otherwise infringing products to territories where patent protection exists, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even pursuing and obtaining issued patents in particular jurisdictions, 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 to stop the infringement of patents, if obtained, or the misappropriation of or marketing of competing products in violation of 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, patent protection might not be sought in certain countries, and there will not be a benefit of patent protection in such countries.

Proceedings to enforce patent rights in foreign jurisdictions could result in substantial costs and divert efforts and attention from other aspects of our business, could put patents at risk of being invalidated or interpreted narrowly, could put patent applications at risk of not issuing, and could provoke third parties to assert claims. We, or our licensees, may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that developed or licensed.

If we, or our licensees, do not obtain additional protection under the Drug Price Competition and Patent Term Restoration Act of 1984, or 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 owned 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, an extension might not be granted 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 unable to obtain a patent term extension or the term of any such extension is less than we request, the duration of patent protection obtained for our product candidates may not provide any meaningful commercial or competitive advantage, 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 product candidates.

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, or 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. 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 product candidates 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 significant market share for our product candidates is obtained, 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, any product candidate revenue or the profitability of that 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 product candidates 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 product candidates 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 product candidates 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. 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 product candidates 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 the provision of supporting scientific, clinical and cost-effectiveness data for the use of our product candidates 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 product candidates. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our product candidates. 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 product candidates 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.

Any product candidates that we may evaluate 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 product candidates;
- the federal Health Insurance Portability and Accountability Act of 1996, or 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, or 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, or 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, or a licensee's 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, or a licensee's ability, to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of our product candidates. In many cases, our product candidates that may be commercialized 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 are developed or commercialized 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 stimulators including ADEMPAS® (riociguat), which has been approved for the treatment of Pulmonary Arterial Hypertension, (PAH) and Chronic Thromboembolic Pulmonary Hypertension (CTEPH) and Verquvo® (vericiguat), which is approved for the treatment of heart failure with reduced ejection fraction. Such sGC products may compete directly with our own product candidates in our non-CNS 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 or our licensees can.

We believe Biogen, Sage, Otsuka, Neumora, Tonix, Neurocrine, Pfizer, atai Life Sciences, Alto Neuroscience, Cerevel, Karuna, PTC Therapeutics, Khondrion B.V, Abliva AB, Reneo, Travere Therapeutics, Dimerix Limited, Vertex Pharmaceuticals, Chinook Therapeutics, Boehringer Ingelheim, Acelyrin, River 3 Renal Corp, Astellas, Pfizer, Eli Lilly, Novartis, AstraZeneca, Bayer and Merck are our most direct competitors with respect to zagociguat, CY3018, praliciguat, and olinciguat.

If our product candidates do not obtain regulatory approvals in 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, then those product candidates 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, nonclinical 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 or our licensees 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 product candidates infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price that could be charged, for any of our product candidates that may be developed and commercialized. 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 product candidates; 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, or a licensee's, 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 or a licensee's 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:

- the customers' ability to obtain reimbursement for our product candidates outside the United States;
- the ability to gain reimbursement in foreign markets at a price that is profitable;
- the 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.

Our ability to generate meaningful revenues in jurisdictions outside of the United States 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 or our licensees 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. If reimbursement of a product candidate, 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 or our licensees may 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

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 development personnel. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. We recently have implemented reduction in force and operate with a relatively small team. The loss of the services of any members of the team and an inability to find suitable replacements could result in operational limitations and harm our business. Pursuant to their employment arrangements, or otherwise, 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. The failure to succeed in nonclinical 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 attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

We may not have a sufficient employee base as needed from time to time, which could disrupt our operations.

As of December 31, 2022, we had 16 full-time employees and we will continue to align our workforce with our business priorities throughout 2022. Whether our operations remain as they are or grow, we may not have a sufficient, or may need to expand our full-time employee base and hire more employees, consultants and contractors. Our management may then need to allocate or divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing ongoing operations or this growth. We may not be able to effectively manage our ongoing operations or 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 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 revenues could be adversely affected and we may not be able to implement our business strategy.

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 any sale thereof, 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 product candidates, 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 Securities Exchange Act of 1934, or The Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the rules and regulations of the Nasdaq Capital Market. We are an "emerging growth company" and a "smaller reporting company." For so long as we remain either an emerging growth company or a smaller reporting 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 Separation; (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, 2022, 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. We have engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There can be no assurances that in future periods we will be able to timely conclude that our internal control over financial reporting is effective as required by Section 404(a).

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 business, prospects, financial condition and results of operations could be harmed, 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, licensees, 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, licensees, 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, or 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 Ownership of Our Common Stock

We could be delisted from Nasdaq, which would seriously harm the liquidity of our stock and ability to raise capital.

On June 1, 2022, the Company received a notice from the Nasdaq Stock Market ("Nasdaq") notifying the Company that, for the last 30 consecutive business days, the closing bid price for the Company's common stock listed on Nasdaq has been below the minimum $1.00 per share required for continued listing on the Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Requirement").

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), the Company was provided a period of 180 calendar days, or until November 28, 2022, to regain compliance with the Bid Price Requirement. The Company did not regain compliance with the Bid Price Requirement by the initial compliance date. On November 29, 2022, however, Nasdaq notified the Company of its eligibility for an additional 180 calendar day period, or until May 29, 2023 (the "Extended Compliance Date"), to regain compliance with the Bid Price Requirement. Nasdaq’s determination was based on the Company meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of the Bid Price Requirement, and the Company's written notice of its intention to cure the deficiency during the second compliance period by effecting a reverse stock split, if necessary. Effective November 25, 2022, the Company transferred its listing of the Company's common stock from the Nasdaq Global Market to the Nasdaq Capital Market, a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market. The Company’s common stock continues to trade under the symbol “CYCN”.

If at any time before May 29, 2023, the bid price of the Company's common stock closes at a $1.00 per share or more for a minimum of 10 consecutive business days, Nasdaq will provide written notification to the Company that it has regained compliance with the Bid Price Requirement. If the Company does not regain compliance with the Bid Price Requirement by the end of the second compliance period, the Company's stock will be subject to delisting.

The Company intends to monitor the closing bid price of its common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Requirement, including initiating a reverse stock split. However, there can be no assurance that the Company will be able to regain compliance with the Bid Price Requirement, would receive sufficient shareholder support for a reverse stock split, or will otherwise be in compliance with other Nasdaq Listing Rules.

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 nonclinical studies and clinical studies of our product candidates;
- the commercial performance of our product candidates, 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 product candidates 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;
- sufficiency, 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;
- Nasdaq's rules, which impose certain continued listing requirements, including a minimum $1 bid price, such that a failure to meet these requirements would lead Nasdaq to take further steps to delist our common stock; 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. 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 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 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 restated 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, or the MBCA, or any action asserting a claim governed by the internal affairs doctrine, in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants. In additional, our articles of organization provide that unless our board of directors consents in writing to the selection of an alternative forum, the U.S. federal district courts shall be the exclusive forum for the resolutions of any complaint asserting a cause of action arising under the U.S. federal securities laws. This exclusive forum provision may limit the ability of our shareholders to bring a claim in a judicial forum that such shareholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against the company and our directors and officers. Alternatively, if a court outside of Massachusetts were to find this exclusive forum provision inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings described above, we may incur additional costs associated with resolving such matters in other jurisdictions, which could harm our business, prospects, financial condition and results of operations.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties

In April 2021 we completed our exit from our prior laboratory and office facilities in Cambridge Massachusetts and moved to an operating model under which we outsource our research and development laboratory work and we are currently leasing office space on an “as-needed” basis.

Item 3. Legal Proceedings

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims, which may have a material adverse effect on our financial position or results of operations.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information for Common Stock

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

Holders of Record

As of February 9, 2023, we had 86 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors.

Unregistered Sales of Equity Securities

None.

Purchase of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. Selected Financial Data.

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

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes and the related Management's Discussion and Analysis of Financial Condition and Results of Operations included in this Annual Report on Form 10-K.

Forward-Looking Information

The following discussion of our financial condition and results of operations should be read in conjunction with the audited consolidated financial statements and the corresponding notes included in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those referenced or set forth under "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors" in Item 1A of this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company on a mission to develop treatments for serious diseases. Zagociguat is a pioneering CNS-penetrant sGC stimulator that has shown rapid improvements across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarkers. sGC stimulators are small molecules that act synergistically with NO as positive allosteric modulators of sGC to boost production of cGMP. cGMP is a key second messenger that, when produced by sGC, regulates diverse and critical biological functions such as mitochondrial function, neuronal function, inflammation and vascular dynamics.

We operate in one reportable business segment—human therapeutics.

Financial Overview

Research and Development Expense. Research and development expenses are incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of the following costs: compensation, benefits and other employee-related expenses, research and development related facilities, third-party contracts relating to nonclinical study and clinical trial activities. All research and development expenses are charged to operations as incurred.

Zagociguat is an orally administered CNS-penetrant sGC stimulator. NO-sGC-cGMP is a fundamental signaling network, including in the brain where it is critical to basic CNS functions. Deficient NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many neurological disorders. As an sGC stimulator, zagociguat amplifies endogenous NO signaling by acting as a positive allosteric modulator to sensitize the sGC enzyme to NO, and increase the production of cGMP. By compensating for deficient NO-sGC-cGMP signaling, zagociguat may have broad therapeutic potential as a treatment for people with serious diseases.

In January 2020, we announced positive results from our Phase 1 first-in-human study that provided the first clinical data supporting the development of zagociguat. The results from this study indicate that zagociguat was well tolerated. Pharmacokinetic data, obtained from both blood and cerebral spinal fluid, support once-daily dosing with or without food and demonstrated zagociguat penetration of the blood-brain-barrier with concentrations in the CSF expected to be pharmacologically active.

In October 2020, we announced positive topline results from our zagociguat Phase 1 translational pharmacology study in healthy elderly participants. Treatment with zagociguat for 15 days in this 24-subject study confirmed and extended results seen in the earlier first-in-human Phase 1 study: once-daily oral treatment demonstrated blood-brain-barrier penetration with expected CNS exposure and target engagement. Results also showed significant improvements in neurophysiological and objective performance measures as well as decreases in inflammatory biomarkers associated with aging and neurodegenerative diseases. Zagociguat was safe and generally well tolerated in the study. These results, together with nonclinical data, support continued development of zagociguat as a potential new medicine for serious CNS diseases.

In June 2022, we announced positive topline clinical data for zagociguat in our signal-seeking clinical study for the potential treatment of MELAS. In this open-label, single-arm study of the oral, once-daily sGC stimulator in eight adults aged 18 or older with MELAS, improvements were seen across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarkers such as lactate and GDF-15, a broad panel of inflammatory biomarkers, cerebral blood flow, and functional connectivity between neural networks. These positive effects after 29 days of dosing were supported by correlations among several endpoints with each other and with zagociguat plasma concentrations. Zagociguat was well tolerated with no serious or severe adverse events and no events leading to discontinuation. Pharmacokinetics were consistent with the Phase 1 studies in healthy volunteers. The positive data from this study supports the potential of zagociguat to provide therapeutic benefit to people living with mitochondrial diseases, including MELAS.

In July 2022, we announced positive topline data from our signal-seeking clinical study of zagociguat for the potential treatment of CIAS. Data from the 14-day, double blind, randomized, placebo-controlled, multiple-ascending-dose study in 48 adults aged 18-50 with stable schizophrenia on a stable, single, atypical antipsychotic regimen demonstrated that once-daily zagociguat was safe and well tolerated, with no reports of serious adverse events, severe adverse events, or treatment discontinuation due to adverse events. We further announced that study data demonstrated a strong effect on cognitive performance after two weeks of 15mg once-daily dosing and that positive movement on inflammatory biomarkers was also observed. These signals on exploratory endpoints are consistent with the pro-cognitive and anti-inflammatory effects of zagociguat observed in preclinical studies and prior clinical trials and support the further development of oral, once-daily zagociguat.

In October 2022, the WHO International Nonproprietary Names committee and the United States Adopted Name Council selected zagociguat as a nonproprietary name for CY6463.

In October 2022, we announced that we had recently capped enrollment in our signal-seeking clinical study of zagociguat for the potential treatment of ADv, to enable the Company to channel its resources to its most urgent priorities in MELAS. Data from the ADv study are expected in the first half of 2023. The ADv study is supported in part by a $2 million grant from the Alzheimer's Association’s Part the Cloud-Gates Partnership Grant Program (the "PTC Grant").

In March 2023, we announced that given the significant capital and capabilities necessary to ensure that the MELAS Phase 2b study is executed efficiently and with the highest quality, and the currently unfavorable capital market conditions, we are actively evaluating the best combination of capital, capabilities, and transactions available to us to advance the development of zagociguat and our other clinical development candidates and to maximize shareholder value.

CY3018 is a CNS-targeted sGC stimulator in preclinical development that preferentially localizes to the brain and has a pharmacology profile that suggests its potential for the treatment of neuropsychiatric diseases and disorders.

Praliciguat is an orally administered, once-daily systemic sGC stimulator. On June 3, 2021, we entered into a license agreement with Akebia relating to the exclusive worldwide license to Akebia of our rights to the development, manufacture, medical affairs and commercialization of pharmaceutical products containing praliciguat and other related products and forms, thereof enumerated in such agreement. Cyclerion is eligible to receive up to $225 million in pre-commercial milestones and total potential future development, regulatory, and commercialization milestone payments could result in up to $585 million. Cyclerion is also eligible to receive tiered, sales-based royalties ranging from single-digit to high-teen percentages.

Olinciguat is an orally administered, once-daily, vascular sGC stimulator that was evaluated in a Phase 2 study of participants with sickle cell disease. We released topline results from this study in October 2020. We continue to work to out-license olinciguat to an entity with strong cardiovascular and/or cardiopulmonary capabilities.

The following table summarizes our research and development expenses, employee and facility related costs allocated to research and development expense, and discovery and pre-clinical phase programs, for the years

ended December 31, 2022 and 2021. The product pipeline expenses relate primarily to external costs associated with nonclinical studies and clinical trial costs, which are presented by development candidates.

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Product pipeline external costs:		
Zagociguat	$ 13,629	$ 12,396
CY3018	4,009	3,310
Discovery research	663	551
Total product pipeline external costs	18,301	16,257
Personnel and related internal costs	10,237	11,374
Facilities and other	2,955	10,005
Total research and development expenses	$ 31,493	$ 37,636

Securing regulatory approvals for new drugs is a lengthy and costly process. Any failure by us to obtain, or any delay in obtaining, regulatory approvals would materially adversely affect our product candidate development efforts and our business overall.

Given the inherent uncertainties of pharmaceutical product development, we cannot estimate with any degree of certainty how our programs will evolve, and therefore the amount of time or money that would be required to obtain regulatory approval to market them. As a result of these uncertainties surrounding the timing and outcome of any approvals, we are currently unable to estimate precisely when, if ever, our discovery and development candidates will be approved. We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data.

The successful development of our product candidates is highly uncertain and subject to a number of risks including, but not limited to:

- The continuing impact of COVID-19, which could continue to adversely affect our programs and operations, including our development activities, corporate development, and other activities.
- Cyclerion works closely with its clinical trial sites and investigators to deliver trials in a manner consistent with the safety of study participants and healthcare professionals.
- The duration of clinical trials may vary substantially according to the type and complexity of the product candidate and may take longer than expected.
- There is substantial doubt regarding our ability to continue as a going concern. We will need to raise additional funding, which may not be available on acceptable terms, or if at all. Failure to obtain necessary capital may force us to delay, limit or terminate our development efforts or other operations.
- The United States FDA and comparable agencies outside the United States impose substantial and varying requirements on the introduction of therapeutic pharmaceutical products, which typically require lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures.
- Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activity. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.
- The duration and cost of discovery, nonclinical studies and clinical trials may vary significantly over the life of a product candidate and are difficult to predict.
- The costs, timing and outcome of regulatory review of a product candidate may not be favorable, and, even if approved, a product may face post-approval development and regulatory requirements.
- The emergence of competing technologies and products and other adverse market developments may reduce or eliminate the potential value of our pipeline.

As a result of the factors listed above, including the factors discussed under the "Risk Factors" section in Item 1A of this Annual Report on Form 10-K, we are unable to determine the duration and costs to complete current or future nonclinical and clinical stages of our product candidates, including as licensed to third parties, or when, or to what extent, we may generate revenues from the commercialization and sale of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the data from the studies of each product candidate, the competitive landscape and ongoing assessments of such product candidate's commercial potential.

General and Administrative Expense. General and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, business development, and human resource functions. Other costs include the legal costs of pursuing patent protection of our intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting and legal services. We record all general and administrative expenses as incurred.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with GAAP. The preparation of these financial statements requires us to make certain estimates and assumptions that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the amounts of expenses during the reported periods. We base our estimates on our historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from our estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

We believe that our application of accounting policies requires significant judgments and estimates on the part of management and is the most critical to aid in fully understanding and evaluating our reported financial results. Our significant accounting policies are more fully described in Note 2, *Summary of Significant Accounting Policies*, of the consolidated financial statements elsewhere in this Annual Report on Form 10-K.

All research and development expenses are expensed as incurred. We defer and capitalize nonrefundable advance payments we make for research and development activities until the related goods are received or the related services are performed. See Note 2, *Summary of Significant Accounting Policies*, of the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Results of Operations

The revenue and expenses reflected in the consolidated financial statements may not be indicative of revenue and expenses that will be incurred by us in the future. The following discussion summarizes the key factors we believe are necessary for an understanding of our consolidated financial statements.

Revenues and Expenses

	Year Ended December 31,		Change	
	2022	2021	$	%
	(dollars in thousands)			
Revenues:				
Revenue from license agreement	$ —	$ 3,000	$ (3,000)	(100)%
Revenue from development agreement	297	320	(23)	(7)%
Revenue from grants	1,328	622	706	114%
Total revenues	1,625	3,942	(2,317)	(59)%
Cost and expenses:				
Research and development	31,493	37,636	(6,143)	(16)%
General and administrative	14,504	20,620	(6,116)	(30)%
Loss on lease termination	—	881	(881)	(100)%
Total cost and expenses	45,997	59,137	(13,140)	(22)%
Loss from operations	(44,372)	(55,195)	10,823	(20)%
Gain on Extinguishment of Debt	—	3,564	(3,564)	(100)%
Interest and other income (expenses), net	294	(16)	310	(1938)%
Net loss	$ (44,078)	$ (51,647)	$ 7,569	(15)%

Revenues. The decrease in revenue of approximately $2.3 million for the year ended December 31, 2022, compared to the year ended December 31, 2021, can be attributed to receiving $3.0 million in revenue from the Akebia License Agreement in 2021 (see Note 13), and offset by approximately $0.7 million in revenue associated with the PTC Grant (see Note 14).

Research and development expenses. The decrease in research and development expenses of approximately $6.1 million for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily driven by a decrease of approximately $1.0 million in non-cash stock-based compensation, a decrease of approximately $2.6 million in the Company's reduced total leased premises, approximately $4.2 million related to a non-cash write-off of leasehold improvements related to the Termination Agreement in 2021, and approximately $0.7 million in salaries and other employee-related costs, partially offset by an increase of approximately $0.4 million related to workforce reduction costs, and approximately $2.0 million in external research costs. The increase in external research costs was primarily due to an increase of approximately $1.2 million in clinical trial costs for zagociguat in MELAS, CIAS and ADv, approximately $0.7 million associated with IND-enabling activities for CY3018, and approximately $0.1 million related to discovery costs.

General and administrative expenses. The decrease in general and administrative expenses of approximately $6.1 million for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily driven by decreases of approximately $2.3 million in non-cash stock-based compensation, approximately $1.0 million in salaries and other employee-related costs, approximately $2.1 million in facilities and operating costs related to a non-cash write-off of leasehold improvements related to the Termination Agreement in 2021, and approximately $0.7 million in professional services expense.

Loss on lease modification and termination. The loss on lease modification and termination of approximately $0.9 million recorded for the year ended December 31, 2021 is related to the lease termination of the Head Lease at 301 Binney Street in Cambridge, Massachusetts that was executed on April 30, 2021.

Gain on Extinguishment of Debt. The gain on extinguishment of debt of $3.5 million recorded in the year ended December 31, 2021 represents the write off of the Paycheck Protection Program ("PPP") loan, which was forgiven by the Small Business Association ("SBA") in November 2021.

Interest and other (expenses) income, net. Interest and other (expenses) income, net increased by approximately $0.3 million for the year ended December 31, 2022, compared to the year ended December 31, 2021 due to the increase of approximately $0.3 million in interest income driven by higher interest rates in the current year as compared to the prior year.

Liquidity and Capital Resources

On September 3, 2020, the Company entered into a sales agreement (the "Sales Agreement") with Jefferies with respect to an at-the-market offering (the "ATM Offering") under the Registration Statement on Form S-3.

Under the ATM Offering, the Company may offer and sell, from time to time at its sole discretion, shares of its common stock, having an aggregate offering price of up to $50.0 million through Jefferies as its sales agent. The Company agreed to pay Jefferies cash commissions of 3.0 percent of the gross proceeds of sales of common stock under the Sales Agreement. The Company has sold 3,353,059 shares of its common stock for net proceeds of $12.5 million under the ATM Offering for the year ended December 31, 2021, since entering into the Sales Agreement with no shares of common stock issued or sold under the ATM Offering during the year ended December 31, 2022. There can be no assurances that the Company will retain or seek to utilize this facility.

On June 7, 2021, we closed on a private placement of our 5,735,988 shares of common stock, pursuant to a Common Stock Purchase Agreement, for total gross proceeds of approximately $18 million. There were no material fees or commissions related to the transaction. The Company intends to use the proceeds to fund working capital and other general corporate purposes.

Our ability to continue to fund our operations and meet capital needs will depend on our ability to generate cash from operations and access to capital markets and other sources of capital, as further described below. We anticipate that our principal uses of cash in the future will be primarily to fund our operations, working capital needs, capital expenditures and other general corporate purposes.

On December 31, 2022, we had approximately $13.4 million of unrestricted cash and cash equivalents. Our cash equivalents include amounts held in U.S. government money market funds. We invest cash in excess of immediate requirements in accordance with our investment policy, which requires all investments held by us to be at least “AAA” rated or equivalent, with a remaining final maturity when purchased of less than twelve months, so as to primarily achieve liquidity and capital preservation.

Continued Nasdaq Listing

On June 1, 2022, the Company received a notice from the Nasdaq Stock Market ("Nasdaq") notifying the Company that, for the last 30 consecutive business days, the closing bid price for the Company's common stock listed on Nasdaq has been below the minimum $1.00 per share required for continued listing on the Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Requirement").

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), the Company was provided a period of 180 calendar days, or until November 28, 2022, to regain compliance with the Bid Price Requirement. The Company did not regain compliance with the Bid Price Requirement by the initial compliance date. On November 29, 2022, however, Nasdaq notified the Company of its eligibility for an additional 180 calendar day period, or until May 29, 2023 (the "Extended Compliance Date"), to regain compliance with the Bid Price Requirement. Nasdaq’s determination was based on the Company meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of the Bid Price Requirement, and the Company’s written notice of its intention to cure the deficiency during the second compliance period by effecting a reverse stock split, if necessary. Effective November 25, 2022, the Company transferred its listing of the Company's common stock from the Nasdaq Global Market to the Nasdaq Capital Market, a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market. The Company’s common stock continues to trade under the symbol “CYCN”.

If at any time before May 29, 2023, the bid price of the Company's common stock closes at a $1.00 per share or more for a minimum of 10 consecutive business days, Nasdaq will provide written notification to the Company that it has regained compliance with the Bid Price Requirement. If the Company does not regain compliance with the Bid Price Requirement by the end of the second compliance period, the Company's stock will be subject to delisting.

The Company intends to monitor the closing bid price of its common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Requirement, including initiating a reverse stock split. However, there can be no assurance that the Company will be able to regain compliance with the Bid Price Requirement, would receive sufficient shareholder support for a reverse stock split, or will otherwise be in compliance with other Nasdaq Listing Rules.

Going Concern

The Company evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. In performing its analysis, management excluded certain elements of its operating plan that cannot be considered probable. Under ASC 205-40, the future receipt of potential funding from future partnerships, equity or debt issuances, and the potential milestones from the Akebia agreement cannot be considered probable at this time because these plans are not entirely within the Company's control and/or have not been approved by the Board of Directors as of the date of these consolidated financial statements.

The Company has incurred recurring losses since its inception, including a net loss of $44.1 million for the year ended December 31, 2022. In addition, as of December 31, 2022, the Company had an accumulated deficit of $259.2 million. The Company expects to continue to generate operating losses for the foreseeable future. The Company expects that its cash, cash equivalents and marketable securities as of December 31, 2022 will not be sufficient to fund operations for at least the next twelve months from the date of issuance of these consolidated financial statements and the Company will need to obtain additional funding. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least 12 months from the date of issuance of these consolidated financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

Cash Flows

The following is a summary of cash flows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Change	
	2022	2021	$	%
	(dollars in thousands)			
Net cash used in operating activities	$ (40,611)	$ (36,517)	$ (4,094)	11 %
Net cash provided by investing activities	$ —	$ 1,457	$ (1,457)	(100)%
Net cash provided by financing activities	$ 29	$ 30,785	$ (30,756)	(100)%

Cash Flows from Operating Activities

Net cash used in operating activities was $40.6 million for the year ended December 31, 2022 compared to $36.5 million for the year ended December 31, 2021. The increase in net cash used in operations of $4.1 million primarily relates to the non-cash leasehold improvement write off of $6.3 million, non-cash loss on lease termination of $0.9 million in the prior year, a decrease of non-cash stock-based compensation and other non-cash items of $3.8 million in the current year and an increase in working capital accounts of $4.3 million, partially offset by a decrease in our net loss of $7.6 million and non-cash gain on extinguishment of debt for $3.6 million in the prior year.

Cash Flows from Investing Activities

Net cash provided by investing activities was $1.5 million from cash received from sale of lab equipment in 2021.

Cash Flows from Financing Activities

Net cash provided by financing activities of $30.8 million for the year ended December 31, 2021 was related to the June 2021 Equity Private Placement of $18 million, net proceeds from the ATM Offering of $12.5 million and proceeds from ESPP shares of $0.3 million.

Debt – Paycheck Protection Program

On April 21, 2020, we received loan proceeds in the amount of approximately $3.5 million pursuant to a promissory note agreement (the "Promissory Note") with a bank under the Paycheck Protection Program ("PPP") of which certain key terms were adjusted by the Paycheck Protection Program Flexibility Act ("PPPFA"). The Promissory Note had an initial loan maturity of April 20, 2022, a stated interest rate of 1.0% per annum, and had payments of principal and interest that were due monthly after an initial deferral period where interest accrued, but no payments were due. Under the PPPFA, the initial deferral may be extended from six up to ten months and the loan maturity may be extended from two to five years. The Promissory Note provided for customary events of default, including, among others, those relating to failure to make payment when due and breaches of representations. The loan is subject to all the terms and conditions applicable under the PPPFA and is subject to review by the Small Business Association ("SBA") for compliance with program requirements.

In August 2021, the Company applied with the SBA for forgiveness of the PPP loan and was notified on November 4, 2021, that the SBA has approved our application to forgive the entire amount of the loan and accrued interest. In November 2021, the Company recorded a gain on extinguishment of debt of $3.6 million representing the principal and accrued interest for the PPP Loan.

Funding Requirements

We expect our expenses to fluctuate as we engage in preclinical activities and clinical trials of our product candidates, continue to maintain out-license opportunities and seek to broaden our portfolio through in-licensing of complementary CNS assets. Based on our cash and cash equivalents position as of December 31, 2022 and our planned operating expenses and capital expenditure requirements there is substantial doubt regarding our ability to continue as a going concern for a period of one year after the date of this Annual Report on Form 10-K. We will need to raise additional capital in upcoming periods, which may not be available on acceptable terms, if at all. Failure to obtain necessary capital when needed may delay current development of our product candidates, halt new development phases, or other operations.

Because of the many risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our working capital requirements. Our expenses will fluctuate, and our future funding requirements will depend on, and could increase or decrease significantly as a result of, many factors, including the:

- scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- costs, timing and outcome of regulatory review of our product candidates;
- costs of future activities, including medical affairs, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- cost and timing of necessary actions to support our strategic objectives;
- costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any.

A change in any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing of the development of that product candidate.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, outstanding equity ownership may be materially diluted, and the terms of securities sold in such transactions could include liquidation or other preferences that adversely affect the rights of holders of common stock. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, debt financing would result in increased fixed payment obligations.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

If we are unable to raise additional funds when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Commitments and Obligations

Tax-related Obligations

We exclude assets, liabilities or obligations pertaining to uncertain tax positions from our summary of contractual commitments and obligations as we cannot make a reliable estimate of the period of cash settlement with the respective taxing authorities. As of December 31, 2022, we had no uncertain tax positions.

Other Funding Commitments

As of December 31, 2022, we had, and continue to have, several ongoing studies in various clinical trial stages. Our most significant clinical trial spending is with clinical research organizations, or CROs. The contracts with CROs generally are cancellable, with notice, at our option and do not have any significant cancellation penalties.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, that would have been established for the purpose of facilitating off-balance sheet arrangements (as that term is defined in Item 303(a)(4)(ii) of Regulation S-K) or other contractually narrow or limited purposes. As such, we are not exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in those types of relationships. We enter into guarantees in the ordinary course of business related to the guarantee of our own performance.

New Accounting Pronouncements

For a discussion of new accounting pronouncements see Note 2, *Summary of Significant Accounting Policies*, of the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

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

Item 8. Financial Statements and Supplementary Data.

The information required by this Item 8 is set forth in our financial statements included in Part IV, Item 15 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

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

With respect to the year ended December 31, 2022, under the supervision and with the participation of our management, we conducted an evaluation of the effectiveness of the design and operations of our disclosure controls and procedures. Based upon this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2022 to provide reasonable assurance that the information required to be disclosed by us in this Annual Report was (a) reported within the time periods specified by SEC rules and regulations and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of consolidated financial statements for external purposes in accordance with U.S. generally accepted accounting principles ("GAAP"). Internal control over financial reporting is a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

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

Management assessed our internal control over financial reporting as of December 31, 2022, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Management's assessment included evaluation of elements such as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies, and our overall control environment.

Based on this assessment, management has concluded that our internal controls over financial reporting were effective as of December 31, 2022 and provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with GAAP. We reviewed the results of management's assessment with the Audit Committee of our Board of Directors.

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Our report was not subject to attestation by our independent registered public accounting firm pursuant to the rules of the Securities and Exchange Commission for "emerging growth companies" that permit us to provide only management's report in this report.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the fiscal year ended December 31, 2022 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Internal Controls

In designing and evaluating the disclosure controls and procedures, management does not expect that our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control systems are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

Item 9B. Other Information.

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections.

Not applicable.

PART III

We intend to file a definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, or the Proxy Statement, with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2023 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," "Executive Officers" and "Section 16(a) Beneficial Ownership Reporting Compliance" and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Proxy Statement under the captions "Executive Compensation" and "Director Compensation" and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans" and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Proxy Statement under the captions "Transactions with Related Persons" and "Independence of the Board of Directors" and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our Proxy Statement under the caption "Ratification of Selection of Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements

See the Index to Consolidated Financial Statements in the Financial Statements Section beginning on page F-1 of this Annual Report on Form 10-K.

(a)(2) Financial Statement Schedules

All financial statement schedules have been omitted as they are not required, not applicable, or the required information is included in the financial statements or notes to the financial statements.

(a)(3) Exhibits

EXHIBIT INDEX

Exhibit No.	Description
2.1	Separation Agreement, dated March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion 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 Cyclerion 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 Cyclerion 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	Description of Securities Registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended
10.1	Tax Matters Agreement, dated March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc. (incorporated by reference to Exhibit 10.3 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787))
10.2	Employee Matters Agreement, dated March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc. (incorporated by reference to Exhibit 10.4 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787))
10.3	Development Agreement, dated April 1, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc. (incorporated by reference to Exhibit 10.5 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787))
10.4	Intellectual Property License Agreement, dated April 1, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc. (incorporated by reference to Exhibit 10.6 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787))
10.5+	Form of Indemnification Agreement between Cyclerion Therapeutics, Inc. and individual directors and officers (incorporated by reference to Exhibit 10.7 to Form 10 filed on January 28, 2019 (File No. 001-38787))
10.6+	Offer Letter, effective April 1, 2019, by and between Cyclerion Therapeutics, Inc. and Peter M. Hecht, Ph.D. (incorporated by reference to Exhibit 10.11 to Current Report on Form 8-K filed on April 2, 2019 (File No. 001-38787))
10.7+	Offer Letter, effective April 1, 2019, by and between Cyclerion Therapeutics, Inc. and Anjeza Gjino

10.8+	Offer Letter, effective April 1, 2019, by and between Cyclerion Therapeutics, Inc. and Cheryl Gault (incorporated by reference to Exhibit 10.1 to Quarterly Report on Form 10-Q filed on May 4, 2022 (File No. 001-38787))
10.9+	Amended and Restated Recognition Bonus Agreement, dated December 21, 2022, by and between Cyclerion Therapeutics, Inc. and Anjeza Gjino
10.10+	Amended and Restated Recognition Bonus Agreement, dated December 21, 2022, by and between Cyclerion Therapeutics, Inc. and Cheryl Gault
10.11+	Cyclerion Therapeutics, Inc. 2019 Employee Stock Purchase Plan (incorporated by reference to Exhibit 4.3 to Registration Statement on Form S-8 filed on March 29, 2019 (File No. 333-230615))
10.12+	Cyclerion Therapeutics, Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 4.4 to Registration Statement on Form S-8 filed on March 29, 2019 (File No. 333-230615))
10.13+	Form of Stock Option Agreement under the Cyclerion Therapeutics, Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 10.10 to Form 10 filed on March 4, 2019 (File No. 001-38787))
10.14+	Form of Non-Employee Director Restricted Stock Agreement under the Cyclerion Therapeutics, Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to Form 10 filed on March 4, 2019 (File No. 001-38787))
10.15+	Form of Restricted Stock Unit Agreement under the Cyclerion Therapeutics, Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to Form 10 filed on March 4, 2019 (File No. 001-38787))
10.16+	Cyclerion Therapeutics, Inc. Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan and forms of agreement thereunder (incorporated by reference to Exhibit 4.5 to Registration Statement on Form S-8 filed on March 29, 2019 (File No. 333-230615))
10.17+	Cyclerion Therapeutics, Inc. Executive Severance Plan (incorporated by reference to Exhibit 10.1 to Quarterly Report on Form 10-Q filed on August 9, 2022 (File No. 001-38787))
10.18+	Non-Employee Director Compensation Policy (amended and restated as of December 17, 2021) (incorporated by reference to Exhibit 10.6 to Quarterly Report on Form 10-Q filed on May 4, 2022 (File No. 001-38787))
10.19	Open Market Sale Agreement, dated September 3, 2020, by and between Cyclerion Therapeutics, Inc. and Jefferies LLC (incorporated by reference to Exhibit 10.1 to Current Report on Form 8-K filed on September 3, 2020 (File No. 001-38787))
10.20*	License Agreement, dated as of June 3, 2021, by and between Cyclerion Therapeutics, Inc. and Akebia Therapeutics, Inc (incorporated by reference to Exhibit 10.2 to Quarterly Report on Form 10-Q filed on July 29, 2021 (File No. 001-38787))
10.21	Common Stock Purchase Agreement, dated as of June 3, 2021, by and between Cyclerion Therapeutics, Inc. and the Investors named therein (incorporated by reference to Exhibit 10.1 to Registration Statement on Form S-3 filed on June 16, 2021 (File No. 333-257145)).
21.1	List of Subsidiaries
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
31.1	Certificate of Chief Executive Officer (Principal Executive Officer) pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certificate of Chief Financial Officer (Principal Financial Officer) pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certificate of Chief Executive Officer (Principal Executive Officer) pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

32.2	Certificate of Chief Financial Officer (Principal Executive Officer) pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File

+ Indicates a management contract or compensatory plan.
* Certain portions of this exhibit (indicated by asterisks) have been omitted because they are not material and are the type that the Registrant treats as private or confidential.

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrants have duly caused this report to be signed on their behalf by the undersigned, thereunto duly authorized, on March 22, 2023.

CYCLERION THERAPEUTICS, INC.

By: /s/ Peter Hecht
Peter M. Hecht
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Peter M. Hecht and Anjeza Gjino, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Cyclerion Therapeutics, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 22, 2023.

Signature	Title
/s/ Peter Hecht Peter M. Hecht	Chief Executive Officer (Principal Executive Officer)
/s/ Anjeza Gjino Anjeza Gjino	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
/s/ Errol De Souza Errol De Souza	Director
/s/ George Conrades George Conrades	Director
/s/ Marsha Fanucci Marsha Fanucci	Director
/s/ Ole Isacson Ole Isacson	Director
/s/ Stephanie Lovell Stephanie Lovell	Director
/s/ Terrance McGuire Terrance McGuire	Director

/s/ Michael Mendelsohn	
Michael Mendelsohn	Director
/s/ Steven Hyman	
Steven Hyman	Director

Index to Consolidated Financial Statements of Cyclerion Therapeutics, Inc.

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Cyclerion Therapeutics, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, has limited financial resources, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

We have served as the Company's auditor since 2018.
Boston, Massachusetts
March 22, 2023
/s/ Ernst & Young LLP

Cyclerion Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands except share and per share data)

	December 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 13,382	$ 53,961
Accounts receivable	96	100
Prepaid expenses	805	928
Other current assets	537	468
Total current assets	14,820	55,457
Property and equipment, net	—	65
Operating lease right-of-use asset	1,218	1,402
Other assets	2,041	2,407
Total assets	$ 18,079	$ 59,331
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,970	$ 1,828
Accrued research and development costs	2,275	6,353
Accrued expenses and other current liabilities	2,382	2,904
Total current liabilities	7,627	11,085
Commitments and contingencies (Note 6)	—	—
Stockholders' equity		
Common stock, no par value, 400,000,000 shares authorized and 43,518,724 issued and outstanding at December 31, 2022 and 400,000,000 shares authorized and 43,410,185 issued and outstanding at December 31, 2021	—	—
Paid-in capital	269,626	263,345
Accumulated deficit	(259,154)	(215,076)
Accumulated other comprehensive loss	(20)	(23)
Total stockholders' equity	10,452	48,246
Total liabilities and stockholders' equity	$ 18,079	$ 59,331

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

Cyclerion Therapeutics, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands except per share data)

	Year Ended December 31,	
	2022	2021
Revenues:		
Revenue from license agreement	$ —	$ 3,000
Revenue from development agreement	297	320
Revenue from grants	1,328	622
Total revenues	1,625	3,942
Cost and expenses:		
Research and development	31,493	37,636
General and administrative	14,504	20,620
Loss on lease termination	—	881
Total cost and expenses	45,997	59,137
Loss from operations	(44,372)	(55,195)
Gain on extinguishment of debt	—	3,564
Interest and other income (expenses), net	294	(16)
Net loss	$ (44,078)	$ (51,647)
Net loss per share:		
Basic and diluted net loss per share	$ (1.01)	$ (1.32)
Weighted average shares used in calculating:		
Basic and diluted net loss per share	43,469	39,144
Other comprehensive loss:		
Net loss	$ (44,078)	$ (51,647)
Other comprehensive loss:		
Foreign currency translation adjustment gain	3	4
Comprehensive loss	$ (44,075)	$ (51,643)

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

Cyclerion Therapeutics, Inc.
Consolidated Statements of Stockholders' Equity
(In thousands except share data)

	Common Stock		Paid-in capital	Accumulated deficit	Accumulated other comprehensive loss	Total Stockholders' equity
	Shares	Amount				
Balance at December 31, 2020	34,047,300	$ —	$ 222,949	$ (163,429)	$ (27)	$ 59,493
Net loss	—	—	—	(51,647)	—	(51,647)
Issuance of common stock - 2021 equity private placement and ATM	9,089,047		30,503	—		30,503
Issuance of common stock upon exercise of stock options, RSUs and employee stock purchase plan	273,838	—	282	—	—	282
Share-based compensation expense related to issuance of stock options and RSUs to employees and employee stock purchase plan	—	—	7,915	—	—	7,915
Share-based compensation expense related to issuance of stock options and RSUs to non-employees	—	—	1,696	—	—	1,696
Foreign currency translation adjustment	—	—	—	—	4	4
Balance at December 31, 2021	43,410,185	$ —	$ 263,345	$ (215,076)	$ (23)	$ 48,246
Net loss	—	—	—	(44,078)	—	(44,078)
Issuance of common stock upon exercise of stock options, RSUs and employee stock purchase plan	108,539	—	29	—	—	29
Share-based compensation expense related to issuance of stock options and RSUs to employees and employee stock purchase plan	—	—	5,091	—	—	5,091
Share-based compensation expense related to issuance of stock options and RSUs to non-employees	—	—	1,161	—	—	1,161
Foreign currency translation adjustment	—	—	—	—	3	3
Balance at December 31, 2022	43,518,724	$ —	$ 269,626	$ (259,154)	$ (20)	$ 10,452

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

Cyclerion Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2022	**2021**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (44,078)	$ (51,647)
Adjustments to reconcile net loss to net cash (used in) operating activities:		
Depreciation and amortization	65	472
Net loss on disposal of property and equipment	—	6,322
Loss on lease termination	—	881
Gain on extinguishment of debt	—	(3,564)
Share-based compensation expense	6,252	9,611
Changes in operating assets and liabilities:		
Accounts receivable	4	(100)
Related party accounts receivable	—	127
Prepaid expenses	123	(112)
Other current assets	(69)	1,244
Operating lease assets	184	(59)
Other assets	366	366
Accounts payable	1,142	679
Related party accounts payable	—	(286)
Accrued research and development costs	(4,078)	4,932
Operating lease liabilities	—	(1,048)
Accrued expenses and other current liabilities	(522)	(4,335)
Net cash (used in) operating activities	(40,611)	(36,517)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	—	(7)
Proceeds from sale of property and equipment	—	1,464
Net cash provided by investing activities	—	1,457
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from equity private placement and ATM	—	30,503
Proceeds from exercises of stock options and ESPP	29	282
Net cash provided by financing activities	29	30,785
Effect of exchange rate changes on cash and cash equivalents	3	4
Net decrease in cash and cash equivalents	(40,579)	(4,271)
Cash and cash equivalents, beginning of period	53,961	58,232
Cash and cash equivalents, end of period	$ 13,382	$ 53,961

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

1. Nature of Business

Nature of Operations

Cyclerion Therapeutics, Inc. (“Cyclerion”, the “Company” or “we”) is a biopharmaceutical company on a mission to develop treatments for serious diseases. Our lead internal asset, zagociguat, is a pioneering, central nervous system ("CNS")-penetrant, soluble guanylate cyclase ("sGC") stimulator that has shown rapid improvements across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarkers. sGC stimulators are small molecules that act synergistically with nitric oxide ("NO") as positive allosteric modulators of sGC to boost production of cyclic guanosine monophosphate ("cGMP"). cGMP is a key second messenger that, when produced by sGC, regulates diverse and critical biological functions such as mitochondrial function, neuronal function, inflammation, and vascular dynamics.

Cyclerion GmbH, a wholly owned subsidiary, was incorporated in Zug, Switzerland on May 3, 2019. The functional currency is the Swiss franc.

Cyclerion Securities Corporation, a wholly owned subsidiary, was incorporated in Massachusetts on November 15, 2019 and was granted securities corporation status in Massachusetts for the 2019 tax year. Cyclerion Securities Corporation has no employees.

Company Overview

The Company’s mission is to develop treatments for serious CNS diseases.

Zagociguat is an orally administered CNS-penetrant sGC stimulator. As an sGC stimulator, zagociguat acts as a positive allosteric modulator to sensitize the sGC enzyme to NO, increase the production of cGMP, and thereby amplify endogenous NO signaling. By compensating for deficient NO-sGC-cGMP signaling, zagociguat may have broad therapeutic potential as a treatment to improve cognition and function in people with serious CNS diseases.

On January 13, 2020, we announced positive results from our Phase 1 first-in-human study that provided the foundation for continued development of zagociguat. The results from this study indicate that zagociguat was well tolerated. Pharmacokinetic data, obtained from both blood and cerebral spinal fluid ("CSF"), support once-daily dosing, with or without food, and demonstrated zagociguat penetration of the blood-brain-barrier with CSF concentrations expected to be pharmacologically active.

On October 14, 2020, we announced positive topline results from our zagociguat Phase 1 translational pharmacology study in healthy elderly participants. Treatment with zagociguat for 15-days in this 24-subject study confirmed and extended results seen in the earlier first-in-human Phase 1 study: once daily oral treatment demonstrated blood-brain-barrier penetration with expected CNS exposure and target engagement. Results also showed significant improvements in neurophysiological and objective performance measures as well as in inflammatory biomarkers associated with aging and neurodegenerative diseases. Zagociguat was safe and generally well tolerated in this study. These results, together with nonclinical data, supported the continued development of zagociguat as a potential new medicine for serious diseases involving the CNS.

On June 10, 2022, we announced positive topline clinical data for zagociguat in our signal-seeking clinical study for the potential treatment of MELAS. In this open-label, single-arm study of the oral, once-daily sGC stimulator in eight adults aged 18 or older with MELAS, improvements were seen across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarker such as lactate and GDF-15, a broad panel of inflammatory biomarkers, cerebral blood flow, and functional connectivity between neural networks. These positive effects after 29 days of dosing were supported by correlations across several endpoints with each other and with zagociguat plasma concentrations. Zagociguat was well tolerated with no adverse events and no events leading to discontinuation. Pharmacokinetics were consistent with the Phase 1 studies in healthy volunteers. The positive data from this study support the potential of zagociguat to provide therapeutic

benefit to people living with mitochondrial diseases, including Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes ("MELAS").

On July 28, 2022, we announced positive topline data from our signal-seeking clinical study of zagociguat for the potential treatment of Cognitive Impairment Associated with Schizophrenia ("CIAS"). Data from the 14-day, double blind, randomized, placebo-controlled, multiple-ascending-dose study in 48 adults aged 18-50 with stable schizophrenia on a stable, single atypical antipsychotic regimen demonstrate that once-daily zagociguat was safe and well tolerated, with no reports of serious adverse events, severe adverse events, or treatment discontinuation due to adverse events. We further announced that study data demonstrated a strong effect on cognitive performance after two weeks of 15mg once-daily dosing and that positive movement on inflammatory biomarkers was also observed. These signals on exploratory endpoints are consistent with pro-cognitive and anti-inflammatory effects of zagociguat observed in preclinical studies and prior clinical trials and support the further development of oral, once-daily zagociguat.

In October 2022, the WHO International Nonproprietary Names committee and the United States Adopted Name council selected zagociguat as a nonproprietary name for CY6463.

On October 6, 2022, we announced that we had recently capped enrollment in our signal-seeking clinical study of zagociguat for the potential treatment of Alzheimer's disease with vascular pathology ("ADv")..Data from the ADv study are expected in the first half of 2023. The ADv study is supported in part by a $2 million grant from the Alzheimer’s Association’s Part the Cloud-Gates Partnership Grant Program (the "PTC Grant").

On March 22, 2023, we announced that given the significant capital and capabilities necessary to ensure that the MELAS Phase 2b study is executed efficiently and with the highest quality, and the currently unfavorable capital market conditions, we are actively evaluating the best combination of capital, capabilities, and transactions available to us to advance the development of zagociguat and our other clinical development candidates and to maximize shareholder value.

CY3018 is a CNS-targeted sGC stimulator in preclinical development that preferentially localizes to the brain and has a pharmacology profile that suggests its potential for the treatment of neuropsychiatric diseases and disorders.

Praliciguat is an orally administered, once-daily systemic sGC stimulator. On June 3, 2021, we entered into the Akebia License Agreement (as defined below) relating to the exclusive worldwide license to Akebia of our rights to the development, manufacture, medical affairs and commercialization of pharmaceutical products containing praliciguat and other related products and forms thereof enumerated in such agreement. Cyclerion is eligible to receive up to $225 million in pre-commercial milestones and total potential future development, regulatory, and commercialization milestone payments could result in up to $585 million. Cyclerion is also eligible to receive tiered, sales-based royalties ranging from single-digit to high-teen percentages.

Olinciguat is an orally administered, once-daily, vascular sGC stimulator that was evaluated in a Phase 2 study of participants with sickle cell disease. We released topline results from this study in October 2020. We continue to work to out-license olinciguat to an entity with strong cardiovascular and/or cardiopulmonary capabilities.

2021 Equity Private Placement

On June 3, 2021, the Company entered into a Common Stock Purchase Agreement (the “2021 Equity Private Placement”) for the private placement of 5,735,988 shares of the Company’s common stock, for total gross proceeds of approximately $18 million. The closing of the 2021 Equity Private Placement occurred on June 7, 2021. The Company did not utilize the services of a placement agent or broker and accordingly incurred no material related transaction fees or commissions.

At-the-Market Offering

On July 24, 2020, the Company filed a Registration Statement on Form S-3 (the "Shelf") with the Securities and Exchange Commission (the "SEC") in relation to the registration of common stock, preferred stock, debt securities, warrants and units of any combination thereof for an aggregate initial offering price not to exceed $150.0 million. The Shelf was declared effective as of July 31, 2020. On September 3, 2020, the Company entered into a Sales Agreement (the "Sales Agreement") with Jefferies LLC ("Jefferies") with respect to an at-the-market offering (the "ATM Offering") under the Shelf. Under the ATM Offering, the Company may offer and sell, from time to time at its sole discretion, shares of its common stock, having an aggregate offering price of up to $50.0 million through Jefferies as its sales agent. The Company will pay to Jefferies cash commissions of 3.0 percent of the gross proceeds of sales of common stock under the Sales Agreement. The Company has sold 3,353,059 shares of its common stock for net proceeds of $12.5 million under the ATM Offering for the year ended December 31, 2021. No shares of common stock have been issued or sold under the ATM Offering during the year ended December 31, 2022.

Basis of Presentation

The consolidated financial statements and the related disclosures have been prepared in accordance with U.S. generally accepted accounting principles. In the opinion of management, the consolidated financial statements reflect all normal recurring adjustments considered necessary for a fair presentation of the Company's financial position and the results of its operations for the fiscal years presented.

The consolidated financial statements include the financial statements of the Company and its wholly owned subsidiaries, Cyclerion GmbH, and Cyclerion Securities Corporation. All significant intercompany accounts and transactions have been eliminated in the preparation of the accompanying consolidated financial statements.

Going Concern

At each reporting period, the Company evaluates whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs and comparing those needs to the current cash and cash equivalent balances. The Company is required to make certain additional disclosures if it concludes substantial doubt exists and it is not alleviated by the Company's plans or when its plans alleviate substantial doubt about the Company's ability to continue as a going concern.

In accordance with Accounting Standards Codification ("ASC") 205-40, Going Concern, the Company evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. In performing its analysis, management excluded certain elements of its operating plan that cannot be considered probable. Under ASC 205-40, the future receipt of potential funding from future partnerships, equity or debt issuances, and the potential milestones from the Akebia agreement cannot be considered probable at this time because these plans are not entirely within the Company's control and/or have not been approved by the Board of Directors as of the date of these consolidated financial statements.

The Company has incurred recurring losses since its inception, including a net loss of $44.1 million for the year ended December 31, 2022. In addition, as of December 31, 2022, the Company had an accumulated deficit of $259.2 million. The Company expects to continue to generate operating losses for the foreseeable future. The

Company expects that its cash, cash equivalents and marketable securities as of December 31, 2022 will not be sufficient to fund operations for at least the next twelve months from the date of issuance of these consolidated financial statements and the Company will need to obtain additional funding. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least 12 months from the date of issuance of these consolidated financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

Notice of Delisting or Failure to Satisfy a Continued Listing Rule or Standard

On June 1, 2022, the Company received a notice from the Nasdaq Stock Market ("Nasdaq") notifying the Company that, for the last 30 consecutive business days, the closing bid price for the Company's common stock listed on Nasdaq has been below the minimum $1.00 per share required for continued listing on the Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Requirement").

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), the Company was provided a period of 180 calendar days, or until November 28, 2022, to regain compliance with the Bid Price Requirement. The Company did not regain compliance with the Bid Price Requirement by the Initial compliance Date. On November 29, 2022, Nasdaq notified the Company that it is eligible for an additional 180 calendar day period, or until May 29, 2023 (the "Extended Compliance Date"), to regain compliance with the Bid Price Requirement. Nasdaq’s determination was based on the Company meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of the Bid Price Requirement, and the Company’s written notice of its intention to cure the deficiency during the second compliance period by effecting a reverse stock split, if necessary. Effective November 25, 2022, the Company transferred its listing of the Company’s common stock from the Nasdaq Global Market to the Nasdaq Capital Market, a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market. The Company’s common stock continues to trade under the symbol “CYCN”.

If at any time before May 29, 2023, the bid price of the Company's common stock closes at a $1.00 per share or more for a minimum of 10 consecutive business days, Nasdaq will provide written notification to the Company that it has regained compliance with the Bid Price Requirement. If the Company does not regain compliance with the Bid Price Requirement by the end of the second compliance period, the Company's stock will be subject to delisting.

The Company intends to monitor the closing bid price of its common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Requirement, including initiating a reverse stock split. However, there can be no assurance that the Company will be able to regain compliance with the Bid Price Requirement or will otherwise be in compliance with other Nasdaq Listing Rules.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Cyclerion Therapeutics, Inc. and its wholly owned subsidiaries, Cyclerion GmbH and Cyclerion Securities Corporation. All intercompany transactions and balances are eliminated in consolidation.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's Chief Executive Officer who is the chief operating decision maker in

deciding how to allocate resources and in assessing performance. The Company currently operates in one reportable business segment - human therapeutics.

Use of Estimates

The preparation of consolidated financial statements in accordance with U.S. generally accepted accounting principles ("GAAP") requires the Company's management to make estimates and judgments that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the amounts of expenses during the reported periods. On an ongoing basis, the Company's management evaluates its estimates, judgments and methodologies. Significant estimates and assumptions in the consolidated financial statements include those related to revenue, impairment of long-lived assets, valuation procedures for right-of-use ("ROU") assets and operating lease liabilities, income taxes, including the valuation allowance for deferred tax assets, research and development expenses, contingencies, share-based compensation, and going concern. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from these estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

Cash and Cash Equivalents

The Company considers all highly liquid investment instruments with a remaining maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents may consist of money market funds and overnight repurchase agreements. The carrying amount of cash equivalents approximates fair value.

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost, and are depreciated when placed into service using the straight-line method based on their estimated useful lives as follows:

Asset Description	Estimated Useful Life (In Years)
Laboratory equipment	5
Computer and office equipment	3
Furniture and fixtures	7
Software	3

Software costs incurred during the preliminary project stage are expensed as incurred, while costs incurred during the application development stage are capitalized and amortized over the estimated useful life of the software. The Company also capitalizes costs related to specific upgrades and enhancements when it is probable the expenditures will result in additional functionality. Maintenance and training costs related to software obtained for internal use are expensed as incurred.

Costs for capital assets not yet placed into service have been capitalized as construction in progress and are depreciated in accordance with the above guidelines once placed into service. Maintenance and repair costs are expensed as incurred.

Leasehold improvements are amortized over the shorter of the estimated useful life of the asset or the lease term.

Property and equipment that is no longer required for the business is considered disposed of when it ceases to be used. Disposals are either sold or retired and the net book value is removed from the consolidated balance sheet and a corresponding gain or loss on the sale or disposal is recognized as a component of operating expenses in the consolidated statements of operations and comprehensive loss.

Fair Value of Investment Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.
- Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Foreign Currency Translation Adjustment

The functional currency of the Company's foreign subsidiary is its local currency, the Swiss franc. The assets and liabilities of the Company's foreign subsidiary are translated into U.S. dollars at exchange rates in effect at the balance sheet date. Income and expense items are translated at the average exchange rates prevailing during the period. The cumulative translation effect for the Company's foreign subsidiary is included as a foreign currency translation adjustment in the consolidated statements of stockholders' equity and as a component of comprehensive loss in the consolidated statements of operations and comprehensive loss.

The Company's intercompany accounts are typically denominated in the functional currency of the foreign subsidiary. Gains and losses resulting from the re-measurement of intercompany balances are recorded in the consolidated statements of operations.

Accounts Receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices. The Company's receivables primarily relate to amounts earned under a development agreement with Ironwood, licensing agreement, and supply agreement. The Company believes that credit risks associated with these agreements are not significant. To date, the Company has not had significant write-offs of bad debt and the Company did not have an allowance for doubtful accounts as of December 31, 2022 or 2021.

Impairment of Long-Lived Assets

The Company regularly reviews the carrying amount of its long-lived assets to determine whether indicators of impairment may exist, which warrant adjustments to carrying values or estimated useful lives. If indications of impairment exist, projected future undiscounted cash flows associated with the asset are compared to the carrying amount to determine whether the asset's value is recoverable. If the carrying value of the asset exceeds such projected undiscounted cash flows, the asset will be written down to its estimated fair value. There were no significant impairments of long-lived assets for the years ended December 31, 2022 or 2021.

Leases

Effective January 1, 2019, the Company adopted Accounting Standards Codification ("ASC") Topic 842, *Leases* ("ASC 842") using the optional transition method. The adoption of ASC 842 represents a change in accounting principle that aims to increase transparency and comparability among organizations by requiring the

recognition of right-of-use assets and lease liabilities on the balance sheet for both operating and finance leases. In addition, the standard requires enhanced disclosures that meet the objective of enabling financial statement users to assess the amount, timing, and uncertainty of cash flows arising from leases. The reported results for the years ended December 31, 2022 and 2021 reflect the application of ASC 842 guidance.

The recognition of right-of-use assets and lease liabilities related to the Company's operating leases under ASC 842 has had a material impact on the Company's consolidated financial statements.

As part of the ASC 842 adoption, the Company has used certain practical expedients outlined in the guidance. These practical expedients include:

- Account policy election to use the short-term lease exception by asset class;
- Election of the practical expedient package during transition, which includes:
- An entity need not reassess whether any expired or existing contracts are or contain leases.
- An entity need not reassess the classification for any expired or existing leases. As a result, all leases that were classified as operating leases in accordance with ASC 840 are classified as operating leases under ASC 842, and all leases that were classified as capital leases in accordance with ASC 840 are classified as finance leases under ASC 842.
- An entity need not reassess initial direct costs for any existing leases.

The Company had a property lease for its headquarters location at 301 Binney Street, Cambridge, MA (the "Head Lease"). The Company determined if the arrangement was a lease at the inception of the contract. The asset component of the Company's operating leases was recorded as operating lease right-of-use assets, and the liability component was recorded as current portion of operating lease liabilities and operating lease liabilities, net of current portion, in the Company's consolidated balance sheets.

ROU assets and operating lease liabilities are recognized based on the present value of lease payments over the lease term at the commencement date. The Company uses an incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments if an implicit rate of return is not provided with the lease contract. Operating lease right-of-use assets are adjusted for incentives received.

Lease cost was recognized on a straight-line basis over the lease term, and included amounts related to short-term leases. Variable lease costs that do not depend on an index or rate were recognized as incurred.

ROU assets and operating lease liabilities were remeasured upon certain modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate upon lease modification. The difference between the remeasured ROU assets and the operating lease liabilities were recognized as a gain or loss in operating expenses. The Company reviewed any changes to its lease agreements for potential modifications and/or indicators of impairment of the respective ROU asset.

On April 30, 2021, the Company entered into a Termination Agreement (the "Termination Agreement") for its Head Lease as initially amended on February 28, 2020, and further amended on September 15, 2020. Pursuant to the Termination Agreement, the Company surrendered the leased space of approximately 57,000 square feet to the building's landlord. The Company did not pay any termination fees with the Termination Agreement. As a result of the termination of the Head Lease, the related right-of-use asset was written off, the lease liability was derecognized, and the $3.8 million security deposit was returned to the Company and recorded as part of our cash balance. In total, the Company recognized a loss on the termination of the Head Lease of $0.9 million for the year ended December 31, 2021. The loss is included in "General and administrative" expenses on our consolidated statement of operations and comprehensive loss.

On September 15, 2020, the Company entered into a Sublease Termination Agreement (the "Sublease Termination Agreement") to terminate its sublease of 15,700 rentable square feet, of its leased premises under the Head Lease. Under the terms of the Sublease Termination Agreement, the subtenant was relieved of its obligation to provide future cash rental payments to the Company. The agreements requiring the former subtenant to provide

licensed rooms and services to the Company free of charge through the original sublease term survived the sublease termination. The Company gained access to the licensed rooms and services beginning in the third quarter of 2021. The letter of credit security deposit related to the sublease was released.

The Company determined that the Sublease Termination Agreement constituted a non-monetary exchange under ASC 845 Nonmonetary Transactions ("ASC 845") where, in return for the free rooms and the services, the Company agreed to terminate its rights and obligations under the sublease agreement. In accordance with ASC 845, the Company determined that the accounting for the transaction should be based on the fair value of assets or services involved. The Company estimated the fair value of the rooms and services to be approximately $1.5 million and $2.9 million, respectively.

The Company determined that the licensed rooms represent a lease under ASC Topic 842 Leases. The Company obtained control of the rooms in the third quarter of 2021 and the prepaid rooms balance of approximately $1.4 million was reclassified from other assets to a ROU asset. The related lease expense is recognized on a straight-line basis over the lease term of 8.88 years. The Company determined that the licensed services represent a non-lease component, which is recognized separately from the lease component for this asset class. The expense related to the licensed services is recognized on a straight-line basis over the period the services are received. Both the lease expense and services expense are recognized as a component of research and development costs in the consolidated statements of operations and comprehensive loss.

In May 2021 the Company signed a 12-month membership agreement to lease space with WeWork at 501 Boylston Street, Boston, Massachusetts, commencing on August 1, 2021. The agreement was extended for six months on August 1, 2022. The 12-month agreement and 6-month extension are accounted for as short-term leases.

Paycheck Protection Program Loan

On April 21, 2020, the Company received loan proceeds in the amount of approximately $3.5 million pursuant to a promissory note agreement with a bank under the Paycheck Protection Program. The Paycheck Protection Program, established as part of the Coronavirus Aid, Relief and Economic Security Act (“CARES Act”), provides for loans to qualifying businesses for amounts up to 2.5 times of the average monthly payroll expenses of the qualifying business. The Promissory Note had an original loan maturity of April 20, 2022, a stated interest rate of 1.0% per annum, and had payments of principal and interest that were due monthly after an initial six-month deferral period where interest accrued, but no payments were due. The Promissory Note provided for customary events of default, including, among others, those relating to failure to make payment when due and breaches of representations. The loan was subject to all the terms and conditions applicable under the PPP and was subject to review by the SBA for compliance with program requirements, including the Company’s certification that the economic uncertainty, at the time, made the PPP loan request necessary to support ongoing operations. On October 2, 2020, the SBA issued procedural guidance with respect to PPP loans and changes in ownership and the Company believes that it is compliant with respect to the 2020 Equity Private Placement and the ATM Offering.

In June 2020, the Payroll Protection Program Flexibility Act was signed into law adjusting certain key terms of loans issued under the PPP. In accordance with the PPPFA, the initial deferral period may be extended from six to up to ten months and the loan maturity may be extended from two to five years. The PPPFA also provided for certain other changes, including the extent to which the loan may be forgiven.

The loan’s principal and accrued interest were forgivable to the extent that the proceeds were used for eligible purposes, subject to certain limitations, and that the Company maintained its payroll levels over a twenty-four-week period following the loan date. The loan forgiveness amount may have been reduced if the Company terminated employees or reduced salaries during the twenty-four-week period. PPP loans are subject to audit and the SBA has indicated that companies that received over $2 million in proceeds should expect an audit. The Company believes that it has used the proceeds for eligible purposes consistent with the provisions of the PPPFA.

As the legal form of the Promissory Note is a debt obligation, the Company accounted for it as debt under Accounting Standards Codification (ASC) 470, *Debt* and recorded a short-term liability of $3.5 million in the consolidated balance sheets upon receipt of the loan proceeds. The Company accrued interest over the term of the loan and did not record additional interest at a market rate because the guidance on imputing interest in ASC 835-30, *Interest* excludes transactions where interest rates are prescribed by a government agency. Approximately $0.1 million of interest expense has been recognized within interest and other income, net in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021. In August 2021, the Company applied

with the SBA for forgiveness of the PPP loan and was notified on November 4, 2021 that the SBA has approved our application to forgive the entire amount of the loan and accrued interest. The Company recorded a gain on extinguishment of debt of $3.6 million in the December 31, 2021 consolidated statements of operations and comprehensive loss, representing the principal and accrued interest for the PPP Loan.

Revenue

Upon executing a revenue generating arrangement, the Company assesses whether it is probable the Company will collect consideration in exchange for the good or service it transfers to the customer. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), it performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies the performance obligations. The Company must develop assumptions that require significant judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The assumptions that are used to determine the stand-alone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. The Company derives revenue from (1) license agreement and (2) supply agreement which are fully described in Note 13, *License Agreement*.

The Company generated revenue from a Development Agreement with Ironwood, pursuant to which the Company provided certain research and development services with respect to certain of Ironwood's products and product candidates. Such research and development activities were governed by a joint steering committee composed of representatives of both companies. Services performed were invoiced at a mutually agreed upon rate and the initial term of the agreement was two years from the date of Separation and automatically renewed for one year unless either party notified the other at least six months prior to the expiration. Ironwood and the Company agreed that the Development Agreement would not be renewed beyond its initial term which ended on March 31, 2021.

The Company generates revenue from research and development grants under contracts with third parties that do not create customer-vendor relationships. The Company's research and development grants are non-exchange transactions and are not within the scope of ASC Topic 606, Revenue from Contracts with Customers ("ASC 606"). Contribution revenue earned from activities performed pursuant to research and development grants is reported as grant revenue in the Company's consolidated statements of operations. Revenue from these grants is recognized as the Company incurs qualifying expenses as stipulated by the terms of the respective grant. Cash received from grants in advance of incurring qualifying expenses is recorded as deferred revenue. The Company records revenue and a corresponding receivable when qualifying costs are incurred before receiving payment from the grants.

Research and Development Costs

The Company expenses research and development costs to operations as incurred. The Company defers and capitalizes nonrefundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed. The Company estimates the period over which such services will be performed and the level of effort to be expended in each period. If actual timing of performance or the level of effort varies from the estimate, the Company will adjust the amounts recorded accordingly. The Company has not experienced any material differences between accrued or prepaid costs and actual costs since inception.

Research and development expenses are comprised of costs incurred in performing research and development activities, which may include salary, benefits and other employee-related expenses; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; and other outside expenses.

General and Administrative Expenses

The Company expenses general and administrative costs to operations as incurred. General and administrative expense consists of compensation, share-based compensation, benefits and other employee-related expenses for personnel in the Company's administrative, finance, legal, information technology, business development and human resource functions. Other costs include the legal costs of pursuing patent protection of the Company's intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting and legal services.

Income taxes

The Company is primarily subject to U.S. federal and Massachusetts state income taxes. For federal and state income taxes, deferred tax assets and liabilities are recognized based upon temporary differences between the financial statement and the tax basis of assets and liabilities. Deferred income taxes are based upon prescribed rates and enacted laws applicable to periods in which differences are expected to reverse. A valuation allowance is recorded when it is more likely than not that some portion or all of the deferred tax assets will not be realized. Accordingly, the Company provides a valuation allowance, if necessary, to reduce deferred tax assets to amounts that are realizable.

The tax positions taken or expected to be taken in the course of preparing the Company tax returns are required to be evaluated to determine whether the tax positions are "more-likely-than-not" of being sustained by the applicable tax authority. Tax positions not deemed to meet a more-likely-than-not threshold would be recorded as a tax expense in the current year. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. It does not consider the likelihood of whether or not the IRS will review the position. Cyclerion evaluates uncertain tax positions on a quarterly basis and adjusts the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Any changes to these estimates, based on the actual results obtained and/or a change in assumptions, could affect Cyclerion's income tax provision in future periods. There were no uncertain tax positions that require accrual or disclosure in the consolidated financial statements as of December 31, 2022, and 2021. The Company's policy is to recognize interest and penalties related to income tax, if any, in income tax expense. As of December 31, 2022, and 2021, the Company has no accruals for interest or penalties related to income tax matters.

Patent Costs

Patent fees and patent related costs in connection with filing and prosecuting patent applications are expensed as incurred and are classified as general and administrative expenses in the accompanying consolidated financial statements. The Company incurred and recorded as operating expense legal and other fees related to patents of approximately $1.7 million and $1.4 million for the years ended December 31, 2022 and 2021, respectively.

Interest and Other Income, Net

For the year ended December 31, 2022, interest and other income, net consisted of a $0.3 million of interest income related to interest generated from our cash and cash equivalents balances. For the year ended December 31, 2021, interest and other income, net consisted of a de minimis amount of interest income related to interest generated from our cash and cash equivalents balances and a de minimis amount of interest expense related to the PPP loan.

Subsequent Events

The Company considers events or transactions that have occurred after the balance sheet date of December 31, 2022, but prior to the filing of the financial statements with the Securities and Exchange Commission, to provide additional evidence relative to certain estimates or to identify matters that require additional recognition

or disclosure. Subsequent events have been evaluated through the filing of the financial statements accompanying this Annual Report on Form 10-K. See Note 15, *Subsequent Events*.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies that are adopted by the Company as of the specified effective date. Except as discussed elsewhere in the notes to the consolidated financial statements, the Company did not adopt any new accounting pronouncements during the years ended December 31, 2022 and 2021, that had a material effect on its consolidated financial statements.

In June 2016 the FASB issued ASU 2016-13, Financial Instruments-Credit Losses. This standard requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. As a smaller reporting company, ASU 2016-13 will become effective for the Company for fiscal years beginning after December 15, 2022, and early adoption is permitted. The Company is currently evaluating the impact that ASU 2016-13 will have on its financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In May 2021 the FASB issued Accounting Standards Update No. 2021-04, Earnings Per Share ("Topic 260"), Debt-Modifications and Extinguishments ("Subtopic 470-50"), Compensation-Stock Compensation ("Topic 718"), and Derivatives and Hedging-Contracts in Entity's Own Equity ("Subtopic 815-40"): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options, a consensus of the Emerging Issues Task Force ("EITF") , which amends the FASB Accounting Standards Codification ("ASC" or the "Codification") to provide explicit guidance, and, thus, reduce diversity in practice, on accounting by issuers for modifications or exchanges of freestanding equity-classified written call options that remain equity classified after the modification or exchange. This amendment provides that for an entity that presents earnings per share ("EPS") in accordance with Topic 260, the effects of a modification or an exchange of a freestanding equity-classified written call option that is recognized as a dividend should be an adjustment to net income (or net loss) in the basic EPS calculation. The amended guidance effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years, and should be applied prospectively to modifications or exchanges occurring on or after the effective date. The Company adopted ASU 2021-04 in the first quarter of 2022, and the adoption of this standard did not have any impact on the Company's financial position or results of operations.

No other accounting standards known by the Company to be applicable to it that have been issued by the FASB or other standard-setting bodies and that do not require adoption until a future date are expected to have a material impact on the Company's consolidated financial statements upon adoption.

3. Fair Value of Financial Instruments

The Company's cash equivalents are generally classified within Level 1 of the fair value hierarchy. The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy used to determine such fair values as of December 31, 2022 and December 31, 2021 (in thousands):

	Fair Value Measurements as of December 31, 2022:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 12,357	$ —	$ —	$ 12,357
Cash equivalents	$ 12,357	$ —	$ —	$ 12,357

	Fair Value Measurements as of December 31, 2021:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 52,917	$ —	$ —	$ 52,917
Cash equivalents	$ 52,917	$ —	$ —	$ 52,917

During the year ended December 31, 2022 and 2021, there were no transfers between levels. The fair value of the Company's cash equivalents, consisting of money market funds, is based on quoted market prices in active markets with no valuation adjustment.

The Company believes the carrying amounts of its prepaid expenses and other current assets, accounts payable, and accrued expenses approximate their fair value due to the short-term nature of these amounts.

4. Property and Equipment

Property and equipment, net consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Software	$ 2,174	$ 2,214
Computer equipment	7	51
Property and equipment, gross	2,181	2,265
Less: accumulated depreciation and amortization	(2,181)	(2,200)
Property and equipment, net	$ —	$ 65

As of December 31, 2022, and 2021, the Company’s property and equipment was primarily located in Boston, Massachusetts.

Depreciation and amortization expense of the Company’s property and equipment was approximately $0.1 million and $0.5 million for the years ended December 31, 2022 and 2021, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Accrued incentive compensation	$ 238	$ 1,369
Salaries	246	266
Accrued vacation	186	345
Professional fees	835	398
Accrued severance and benefit costs	809	—
Other	68	526
Accrued expenses and other current liabilities	$ 2,382	$ 2,904

6. Commitments and Contingencies

Other Funding Commitments

In the normal course of business, the Company enters into contracts with clinical research organizations and other third parties for clinical and preclinical research studies and other services and products for operating purposes. These contracts are generally cancellable, with notice, at the Company’s option and do not have any significant cancellation penalties.

Guarantees

On September 6, 2018, Cyclerion was incorporated in Massachusetts and its officers and directors are indemnified for certain events or occurrences while they are serving in such capacity.

The Company enters into certain agreements with other parties in the ordinary course of business that contain indemnification provisions. These typically include agreements with directors and officers, business partners, contractors, clinical sites and customers. Under these provisions, the Company generally indemnifies and holds harmless the indemnified party for losses suffered or incurred by the indemnified party as a result of the Company's activities. These indemnification provisions generally survive termination of the underlying agreements. The maximum potential amount of future payments the Company could be required to make under these indemnification provisions is unlimited. However, to date the Company has not incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. As a result, the estimated fair value of these obligations is minimal. Accordingly, the Company did not have any liabilities recorded for these obligations as of December 31, 2022 or December 31, 2021.

7. Leases

On April 30, 2021, the Company entered into a Termination Agreement (the "Termination Agreement") for its Head Lease (the "Head Lease") for the Company's former headquarters located at 301 Binney Street, Cambridge, MA, as initially amended on February 28, 2020, and further amended on September 15, 2020. Pursuant to the Termination Agreement, the Company surrendered the leased space of approximately 57,000 square feet to the building's landlord. The Company did not pay any termination fees in connection with the Termination Agreement. As a result of the termination of the Head Lease, the related right-of-use asset was written off, the lease liability was derecognized, and the $3.8 million security deposit was returned to the Company and recorded as part of our cash balance.

Lease cost was recognized on a straight-line basis over the lease term. For the year ended December 31, 2021, the Company recognized approximately $2.4 million of total lease costs and $0.7 million of variable lease costs, related to the Head Lease. The Company did not record any lease costs related to the Head Lease during the year ended December 31, 2022.

In May 2021 the Company signed a 12-month membership agreement to lease space with WeWork at 501 Boylston Street, Boston, Massachusetts, commencing on August 1, 2021. The agreement was extended for six months on August 1, 2022. The 12-month agreement and 6-month extension are accounted for as short-term leases. The Company recorded $0.3 million and $0.1 million, respectively, in lease expense associated with the membership agreement during the years ended December 31, 2022, and 2021.

Supplemental cash flow information related to leases for the periods reported is as follows:

	Year Ended December 31,	
	2022	2021
Decrease in right-of-use assets related to lease modifications and termination	$ —	$ 42,058
Decrease in operating lease liabilities due to lease modifications and termination	$ —	$ 41,177
Cash paid for amounts included in the measurement of lease liabilities (in thousands)	$ —	$ 1,887
Weighted-average remaining lease term of operating leases (in years)	—	—
Weighted-average discount rate of operating leases	—	—

On September 15, 2020, the Company entered into a Sublease Termination Agreement (the "Sublease Termination Agreement") to terminate its sublease of 15,700 rentable square feet, of its leased premises under the Head Lease. Under the terms of the Sublease Termination Agreement, the subtenant was relieved of its obligation to provide future cash rental payments to the Company. The agreements requiring the former subtenant to provide licensed rooms and services to the Company free of charge through the original sublease term survived the sublease termination. The Company gained access to the licensed rooms and services beginning in the third quarter of 2021. The letter of credit security deposit related to the sublease was released.

The Company determined that the Sublease Termination Agreement constituted a non-monetary exchange under ASC 845 Nonmonetary Transactions (“ASC 845”) where, in return for the free rooms and the services, the Company agreed to terminate its rights and obligations under the sublease agreement. In accordance with ASC 845, the Company determined that the accounting for the transaction should be based on the fair value of assets or services involved. The Company estimated the fair value of the rooms and services to be approximately $1.5 million and $2.9 million, respectively.

The Company determined that the licensed rooms represent a lease under ASC Topic 842 Leases. The Company obtained control of the rooms in the third quarter of 2021 and the prepaid rooms balance of approximately $1.4 million was reclassified from other assets to a ROU asset. The related lease expense is recognized on a straight-line basis over the lease term of 8.88 years. The Company recorded $0.2 million and $0.1 million of lease expense during the years ended December 31, 2022 and 2021, respectively. The Company determined that the licensed services represent a non-lease component, which is recognized separately from the lease component for this asset class. The expense related to the licensed services is recognized on a straight-line basis over the period the services are received. The Company recorded $0.4 million and 0.2 million for the years ended December 31, 2022 and 2021, respectively. Both the lease expense and services expense are recognized as a component of research and development costs in the consolidated statements of operations and comprehensive loss.

8. Share-based Compensation Plans

In 2019, Cyclerion adopted share-based compensation plans. Specifically, Cyclerion adopted the 2019 Employee Stock Purchase Plan (“2019 ESPP”) and the 2019 Equity Incentive Plan (“2019 Equity Plan”). Under the 2019 ESPP, eligible employees may use payroll deductions to purchase shares of stock in offerings under the plan, and thereby acquire an interest in the future of the Company. The 2019 Equity Plan provides for stock options and restricted stock units (“RSUs”).

Cyclerion also mirrored two of Ironwood Pharmaceuticals, Inc. ("Ironwood") existing plans, the Amended and Restated 2005 Stock Incentive Plan (“2005 Equity Plan”) and the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan (“2010 Equity Plan"). These mirror plans were adopted to facilitate the exchange of Ironwood equity awards for Cyclerion equity awards upon the Separation as part of the equity conversion. As a result of the Separation and in accordance with the EMA, employees of both companies retained their existing Ironwood vested options and received a pro-rata share of Cyclerion options, regardless of which company employed them post-Separation. For employees that were ultimately employed by Cyclerion, unvested Ironwood options and RSUs were converted to unvested Cyclerion options and RSUs.

The following table provides share-based compensation reflected in the Company’s consolidated statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	$ 2,915	$ 3,945
General and administrative	3,337	5,666
	$ 6,252	$ 9,611

Stock Options

Stock options granted under the Company’s equity plans generally have a ten-year term and vest over a period of four years, provided the individual continues to serve at the Company through the vesting dates. Options granted under all equity plans are exercisable at a price per share not less than the fair market value of the underlying common stock on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the requisite service period, which is typically the vesting period of each option.

A summary of stock option activity for the year ended December 31, 2022 is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Average Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	7,080,426	$ 10.73	6.9	—
Granted	1,695,303	1.16		
Exercised	—	—		
Cancelled or forfeited	1,463,836	7.14		
Outstanding as of December 31, 2022	7,311,893	$ 9.23	5.8	$ 20
Exercisable at December 31, 2022	5,282,088	$ 11.88	4.8	$ —

During the years ended December 31, 2022 and 2021, the Company granted stock options to purchase an aggregate of 1,695,303 shares and 1,176,250 shares, respectively, at weighted average grant fair values per option share of $0.91 and $2.17 respectively. The total grant fair value of options granted during the years ended December 31, 2022 and 2021 was $1.5 million and $2.6 million, respectively.

The total intrinsic value of options exercised for the year ended December 31, 2021 was $0.1 million. There were no options exercised during the year ended December 31, 2022.

As of December 31, 2022, the unrecognized share-based compensation expense, net of estimated forfeitures, related to all unvested time-based stock options held by the Company's employees is $2.1 million and the weighted average period over which that expense is expected to be recognized is 3.3 years.

The weighted-average Black-Scholes assumptions used in estimating the fair value of the stock options granted by Cyclerion following the Separation during the years ended December 31, 2022 and 2021 were as follows:

	Year ended December 31,	
	2022	2021
Weighted average risk-free interest rate	1.93 %	1.09 %
Expected dividend yield	—	—
Expected option term (in years)	6.0	5.9
Expected stock price volatility	98.90 %	85.45 %

For the years ended December 31, 2022 and 2021, expected volatility was estimated using an average of the historical volatility of the common stock of a group of similar companies that were publicly traded. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

The Company has granted to certain employees performance based options to purchase shares of common stock. These options are subject to performance based milestone vesting. During the year ended December 31, 2022, there were no shares that vested as a result of performance milestone achievements and 50,000 shares vested during the year ended December 31, 2021. The Company recorded a de minimis and no share-based compensation expense related to these performance-based options for the years ended December 31, 2022, and 2021, respectively.

Market-based Stock Options

The Company also has granted to certain employees stock options containing market conditions that vest upon the achievement of specified price targets of the Company's share price for a period through December 31, 2024. Vesting is measured based upon the average closing price of the Company's share price for any thirty consecutive trading days, subject to certain service requirements. Stock compensation cost is expensed on a straight-line basis over the derived service period for each stock price target within the award, ranging from approximately 4.0 to 4.6 years. The Company accelerates expense when a stock price target is achieved prior to the derived service period. The Company does not reverse expense recognized if the share price target(s) are ultimately not achieved but expense is reversed when a stock award recipient has a break in service prior to the completion of the derived service period. As of December 31, 2022, there was $0.1 million of unrecognized compensation costs related to

stock options containing market conditions, which is expected to be recognized over a weighted-average period of 1.2 years.

A summary of stock awards containing market conditions activity for the years ended December 31, 2022 and 2021 is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	450,000	$ 2.01	$ 7.9	$ —
Granted	—	—	—	—
Exercised	—	—	—	—
Cancelled or forfeited	(150,000)	$ 2.01	$ 6.9	$ —
Outstanding as of December 31, 2022	300,000	$ 2.01	6.9	$ —
Exercisable at December 31, 2022	—	$ —	—	$ —

The fair value of stock options containing market conditions is estimated using Monte Carlo simulations. No stock options containing market conditions were granted during the years ended December 31, 2022 and 2021.

Restricted Stock Units

The RSUs generally vest 25% per year on the approximate anniversary of the date of grant until fully vested, provided the employee remains continuously employed with the Company through each vesting date. Shares of the Company's common stock are delivered to the employee upon vesting, subject to payment of applicable withholding taxes. The fair value of all RSUs is based on the market value of the Company's common stock on the date of grant. Compensation expense, including the effect of estimated forfeitures, is recognized over the applicable service period.

A summary of RSU activity for the years ended December 31, 2022 is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested as of December 31, 2021	92,804	$ 13.70
Granted	800,000	0.53
Vested	(53,999)	14.06
Forfeited	(23,218)	13.43
Unvested as of December 31, 2022	815,587	$ 0.77

As of December 31, 2022, the unrecognized share-based compensation expense, net of estimated forfeitures, related to all unvested restricted stock units by the Company's employees is $0.4 million and the weighted-average period over which that expense is expected to be recognized is 0.8 years.

9. Loss per share

Basic and diluted net loss per common share is computed by dividing net loss by the weighted average number of common shares outstanding during the period as follows:

	Year Ended December 31,	
	2022	2021
Numerator:		
Net loss (in thousands)	$ (44,078)	$ (51,647)
Denominator:		
Weighted average shares used in calculating net loss per share — basic and diluted (in thousands)	43,469	39,144
Net loss per share — basic and diluted	$ (1.01)	$ (1.32)

We exclude shares of common stock related to stock options and RSUs from the calculation of diluted net loss per share since the inclusion of such shares would be anti-dilutive. The following table sets forth potential shares that were considered anti-dilutive for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
Stock Options	7,611,893	7,530,426
RSUs	815,587	92,804
	8,427,480	7,623,230

10. Income Taxes

There was no provision for income taxes for the years ended December 31, 2022, and 2021, due to the Company's operating losses and a full valuation allowance on deferred tax assets. Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes.

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows (in thousands):

	Year Ended December 31,	
	2022	2021
U.S.	$ (44,063)	$ (51,686)
International	(15)	39
Loss before benefit from income taxes	$ (44,078)	$ (51,647)
Income tax benefit using U.S. federal statutory rate	$ (9,256)	$ (10,846)
State income taxes, net of federal benefit	(2,693)	(3,631)
Non-deductible share-based compensation	266	(911)
Share-based compensation - shortfalls/(windfalls)	833	946
Permanent differences	14	(420)
PPP loan forgiveness	—	(748)
Tax credits	(1,652)	(805)
Other	3	(9)
Change in valuation allowance	12,485	16,424
	$ —	$ —

The effective income tax rate is based upon the income for the year, the composition of the income in different countries, and adjustments, if any, for the potential tax consequences, benefits or resolutions of audits or other tax contingencies. Our income tax rate in foreign jurisdictions is lower than our income tax rate in the United States.

Deferred tax assets (liabilities) consist of the following as of December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 47,079	$ 43,700
Tax credit carryforwards	9,848	8,044
Share-based compensation	8,354	7,702
Operating lease - liability	—	—
Property and equipment	1	(1)
Capitalized research and development	17,399	11,147
Accruals and reserves	340	91
Other	—	4
Total deferred tax assets	$ 83,021	$ 70,687
Deferred tax liabilities:		
Operating lease - right of use asset	$ (333)	$ (383)
Prepaid sublease termination	(658)	(758)
Total deferred tax liabilities	(991)	(1,141)
Net deferred tax assets	82,030	69,546
Valuation allowance	(82,030)	(69,546)
Net deferred tax assets	$ —	$ —

Management has evaluated the positive and negative evidence bearing upon the possible realization of its deferred tax assets. Management has considered the Company's history of operating losses, in addition to the expected timing of the reversal of existing temporary differences and concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company will not realize the benefit of its deferred tax assets. Accordingly, the net deferred tax assets have been fully reserved at December 31, 2022 and December 31, 2021. Management reevaluates the positive and negative evidence on a quarterly basis.

The valuation allowance increased by approximately $12.5 million during the year ended December 31, 2022 primarily due to increases in capitalized research and development expenses, net operating losses, tax credit carryforwards and deferred tax assets related to share-based compensation.

The Company did not generate net operating loss carryforwards or tax credit carryforwards available for its use until its inception and operation as a standalone legal entity. At December 31, 2022 and 2021, Cyclerion has federal net operating loss carryforwards of approximately $172 million and $160 million, respectively, to offset future federal taxable income that will be carried forward indefinitely until utilized. As of December 31, 2022, and 2021, Cyclerion had state net operating loss carryforwards of approximately $173 million and $159.6 million, respectively, to offset future state taxable income, which will begin to expire in 2040 and will continue to expire through 2042. Cyclerion also had tax credit carryforwards of approximately $10.2 million and $8.4 million as of December 31, 2022 and 2021, respectively, to offset future federal and state income taxes. Federal credits begin to expire in 2040 and will continue to expire through 2041. State credits begin to expire in 2022 and continue through 2034.

The Company’s ability to use its operating loss carryforwards and tax credits to offset future taxable income could be subject to restrictions under Section 382 of the U.S. Internal Revenue Code of 1986, as amended (the “Internal Revenue Code”). These potential restrictions may limit the future use of the operating loss carryforwards and tax credits if certain ownership changes described in the Internal Revenue Code occur. Changes in stock ownership may occur that would create these limitations on the Company’s use of the operating loss carryforwards and tax credits. In such a situation, the Company may be required to pay income taxes, even though significant operating loss carryforwards and tax credits exist.

The Company has not as yet conducted a study of its research and development credit carry forwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations if an adjustment were required.

Upon audit, taxing authorities may challenge all or part of an uncertain income tax position. While Cyclerion has no history of tax audits since its inception on a standalone basis, it may be subject to tax audits by federal and state taxing authorities in the future. Accordingly, Cyclerion regularly assesses the outcome of potential examinations in each of the taxing jurisdictions when determining the adequacy of the amount of unrecognized tax benefit recorded. Cyclerion had no unrecognized tax benefits as of December 31, 2022 and 2021. Cyclerion will recognize interest and penalties, if any, related to uncertain tax positions in income tax expense. As of December 31, 2022 and 2021, no interest or penalties have been accrued. There are no current federal or state income tax audits in progress.

11. Defined Contribution Plan

The Company has established a defined contribution 401(k) Savings Plan which allows eligible employees to contribute from 1% to 100% of their compensation, subject to certain IRS limits. The Company's contributions to the plan are at the sole discretion of the board of directors. Currently, the Company provides a matching contribution of 75% of the employee's contributions, up to $6,000 annually.

Included in compensation expense is approximately $0.2 million and $0.3 million related to the defined contribution 401(k) Savings Plan for the years ended December 31, 2022 and 2021, respectively.

12. Workforce Reduction

2022 Workforce Reduction

On October 6, 2022, the Company began a reduction of its current workforce by thirteen (13) full-time employees to align its resources with its current priorities of focusing on a mitochondrial disease-focused strategy. The workforce reduction was completed in the fourth quarter of 2022.

The Company recorded total costs related to the 2022 Workforce Reduction were approximately $1.3 million, including a de minimis amount of stock-based compensation from the modification of certain share-based equity awards.

The following table summarizes the accrued liabilities activity recorded in connection with the reduction in workforce for the year ended December 31, 2022 (in thousands):

	Amounts accrued at December 31, 2021	Charges	Amount paid	Amounts accrued at December 31, 2022
2022 workforce reduction	$ —	$ (1,327)	$ 518	$ (809)
Total	$ —	$ (1,327)	$ 518	$ (809)

13. License Agreement

Akebia License Agreement

On June 3, 2021, the Company and Akebia entered into a License Agreement (the "Akebia License Agreement") relating to the exclusive worldwide license by the Company to Akebia of our rights to the development, manufacture, medical affairs and commercialization of pharmaceutical products containing the pharmaceutical compound known as praliciguat and other related products and forms thereof enumerated in the

License Agreement (collectively, the “Products”). Pursuant to the Akebia License Agreement, Akebia will be responsible for all future research, development, regulatory, and commercialization activities for the Products.

Akebia paid a $3.0 million up-front payment to the Company upon signing of the License Agreement and the Company is eligible to receive additional milestone cash payments of up to $12.0 million upon initiation of a Phase 2 clinical trial. Further milestone cash payments by Akebia are scheduled in the Akebia License Agreement based on the initiation of Phase 3 clinical trials in the U.S. for Products for first and second indication, for FDA approvals, for approvals in certain other major markets, and for certain sales milestones. In addition to these cash milestone payments, Akebia will pay the Company tiered royalty payments on net sales in certain major markets at percentages ranging from the mid-single digits to the high-teens, subject to certain reductions and offsets.

Pursuant to the Akebia License Agreement, the Company determined the Akebia License Agreement represents a service arrangement under the scope of ASC 606. Given the reversion of the rights under the Akebia License Agreement represents a penalty in substance for a termination by Akebia, the contract term would be the stated term of the License Agreement.

The Company determined that the grant of license to our patents and trademarks, know how transfer, the assignment of regulatory submissions and trademarks and additional knowledge transfer assistance obligations represent a single promise and performance obligation to be transferred to Akebia over time due to the nature of the promises in the contract. The provision of development materials on hand was identified as a separate performance obligation. However, it is immaterial in the context of the contract as the development materials are low value and do not have an alternative use to the Company.

The consideration related to sales-based milestone payments, including royalties, will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license. The Company will re-evaluate the probability of achievement of the milestones and any related constraints each reporting period.

Akebia Supply Agreement

On August 3, 2021, the Company and Akebia entered into a Supply Agreement (the “Supply Agreement”) relating to the manufacturing by the Company of the Initial Supply of the Drug Product and placebo ("Initial Supply") for Akebia's use pursuant to the Akebia License Agreement. Akebia will pay the Company for the manufacturing costs at mutually agreed upon rates.

The Company determined the Supply Agreement has stand-alone value under the scope of ASC 606 and should not be combined with the Akebia License Agreement. Given that the Supply Agreement can be terminated at any time without cause with 30 days notice, the Company deemed the Supply Agreement to be a month-to-month contract. The manufacturing of the Initial Supply by the Company represents a single performance obligation and consideration related to the manufacturing costs will be recognized over time as costs are incurred. The Company recorded approximately $0.3 million and approximately $0.3 million, respectively, for the years ended December 31, 2022 and 2021, as revenue from the Supply Agreement.

14. Grant Revenue

In August 2021, the Company was approved to receive funding from the PTC Grant for the Phase 2 study of CNS sGC stimulation in AD with vascular features. The granting period is July 1, 2021, to December 31, 2022, and the Company will receive an award of up to $2 million. The Company determined that this transaction is non-reciprocal as there is not considered to be a commensurate value exchanged with the Alzheimer's Association as the funding provider. Where commensurate value is not exchanged for goods and services provided, a recipient assesses whether the grant is conditional or unconditional. The Company considered all conditions and barriers associated with this grant and determined the grant is conditional and revenue will be recognized upon achieving certain milestones and incurring internal costs specifically covered by this grant. Under ASC 958-605, revenues will be recognized as the Company incurs expenses related to the PTC Grant.

The Company incurred approximately $1.3 million and approximately $0.6 million of allowable expenses and recognized a corresponding amount of grant revenue for the years ended December 31, 2022 and 2021.

15. Subsequent Events

The Company has evaluated all events and transactions that occurred after the balance sheet date through the date the consolidated financial statements were issued and determined that there were no such events requiring recognition or disclosure in the consolidated financial statements.

Exhibit 4.1

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

General

The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our articles of organization and bylaws, the Annual Report on Form 10-K to which this description is an exhibit, any and all of which may be amended from time to time, and to the applicable provisions of the Massachusetts Business Corporation Act ("MBCA").

Our authorized capital stock consists of 400,000,000 shares of our common stock and 100,000,000 shares of our preferred stock, all of which preferred stock is undesignated. As of March 5, 2020, there were 27,754,894 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Dividend Rights

Subject to preferences that may apply to shares of preferred stock outstanding, holders of outstanding 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.

Voting Rights

Each outstanding share of common stock is entitled to one vote on all matters submitted to a vote of shareholders. Holders of shares of our common stock have no cumulative voting rights.

Preemptive Rights.

Our common stock is not entitled to preemptive or other similar subscription rights to purchase any of our securities.

Conversion or Redemption Rights

Our common stock is neither convertible nor redeemable.

Liquidation Rights

Upon our liquidation, the holders of our common stock will be 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.

Listing

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

Anti-takeover Effects of Our Articles of Organization and Our Bylaws

Our articles of organization and 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 and Special Meetings of Shareholders

Our 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 articles of organization and the 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 bylaws contain 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 will only be 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 our 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 bylaws provide 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 included in our bylaws, including the provision of timely written notice to our Secretary.

Number of Directors and Filling Vacancies and Election of Directors

Our 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 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 and 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.

Exclusive Forum.

Our articles of organization require, to the fullest extent permitted by law, that derivative actions brought in the name of Cyclerion, actions against our directors, officers and employees for breach of a fiduciary duty and other similar actions may be brought only in specified courts in the Commonwealth of Massachusetts. Although we believe this provision benefits us by providing increased consistency in the application of Massachusetts law in the

types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Anti-Takeover Provisions under Massachusetts Law

Provisions Regarding Business Combinations

We are 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 this 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 plan to opt out of this default requirement for a classified board of directors, and expect that all of our directors serve for one-year terms and will be elected annually.

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.

Transfer Agent and Registrar

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

Indemnification of Directors and Officers

Our 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 bylaws also provide that we 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 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 have also entered, or expect to enter, 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.

Part 8 of the MBCA authorizes the provisions, described above, that is contained in our articles of organization and 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.

Exhibit 10.7

3/11/19

Re: Offer of Transfer to Cyclerion

Dear Anjeza:

On behalf of all my colleagues at Cyclerion, I am pleased to provide you with the terms and conditions of your anticipated employment by Cyclerion Therapeutics, Inc., a Massachusetts corporation (the "Company"). As you are aware, the Company intends to separate from Ironwood Pharmaceuticals, Inc. This offer is contingent on the completion of the separation. This offer, if accepted, sets forth the terms of your employment with the Company after the separation. If you accept this offer, it will take effect upon the separation.

1. Position. Your position will be that of VP of Finance, reporting to Bill Huyett. In addition to performing duties and responsibilities associated with such position, from time to time the Company may assign you other duties and responsibilities. As a full-time employee of the Company, you will be expected to devote your full business time and energies to the business and affairs of the Company.

2. Starting Date/Nature of Relationship. It is expected that your employment will start on the separation, anticipated to be 4/1/19. No provision of this offer letter shall be construed to create an express or implied employment contract for a specific period of time. Either you or the Company may terminate the employment relationship at any time and for any reason.

3. Compensation.

    a. Your initial base salary for this exempt position will be paid bi-weekly, equal to $242,100 per year.

    b. You will be eligible for a target bonus of 30% of your base salary, based on achievement of mutually acceptable goals developed by you and your manager, and the Company's achievement of its corporate goals. These goals, and the terms of the target bonus, will be communicated to you at a later date.

4. Benefits.

    a. The benefits in which you are enrolled at Ironwood will transfer with you to Cyclerion. The Company retains the right to change, add or cease any particular benefit. Current benefits include: medical, dental, and vision insurance, disability and life insurance, 401k plan, flexible spending plan, paid time off, and holidays. Details about your Cyclerion benefits, including the impact of payments made toward Ironwood deductibles and out-of-pocket maximums, if applicable, will be provided under separate cover.

    b. As an employee of the Company, you will be entitled to unlimited paid time off (PTO), to be taken pursuant to the Company's PTO policy. By accepting this offer of employment, you agree that your Ironwood accrued vacation balance will be transferred and credited to your employee record at the Company and will be paid out to you upon termination of your employment with the Company.

    c. Your original hire date at Ironwood Pharmaceuticals, Inc of 2/28/11 will be incorporated into your Cyclerion record as your service date.

5. Confidentiality. The Company considers the protection of its confidential information and proprietary materials to be very important. Therefore, as a condition of your employment, you and the Company will become parties to an agreement regarding non-competition, non-solicitation and ownership of intellectual property (as applicable), which has been provided to you herewith.

6. General.

    a. The agreement between you and Cyclerion regarding your use and non-disclosure of Cyclerion confidential information, and regarding non-competition, non-solicitation, and ownership of intellectual property (as applicable) will constitute our entire agreement as to the terms of your employment by the Company and will supersede any prior agreements or understanding, whether in the writing or oral.

    b. As required by law, this offer is subject to satisfactory proof of right to work in the United States.

    c. This letter shall be governed by the laws of the Commonwealth of Massachusetts, without application of its principles of conflict laws.

In addition, by accepting this offer, you represent and warrant to the Company that from and after your start date of employment, you will not be subject to any noncompetition or other agreement prohibiting you from performing services for the Company to the full extent contemplated by this letter. In addition, should you become legally prohibited from performing services for the Company to the full extent contemplated by this letter, or should the Company reasonably believe that you are legally prohibited from performing services to the full extent contemplated by this letter, the Company shall have the right to rescind your offer and/or immediately terminate your employment.

This offer of transition will expire on 3/28/2019 unless accepted by you prior to such date.

We are very excited to build Cyclerion into a great entrepreneurial biopharmaceutical company with you!

Sincerely,

CYCLERION THERAPEUTICS, INC.

/s/ Bill Huyett
Bill Huyett
President (future CFO)

Accepted this 19 day of March 2019
/s/ Anjeza Gjino
Employee Name

Cyclerion Therapeutics, Inc.

December 21, 2022

Anjeza Gjino

Re: Amended and Restated Recognition Bonus Agreement

Dear Anjeza:

This letter agreement (this "Agreement") between you and Cyclerion Therapeutics, Inc. (the "Company") amends and restates the prior retention bonus letter agreement, dated October 3, 2022, between you and the Company, with respect to your opportunity to earn a Recognition Bonus (as defined below). The Company is offering you this opportunity in recognition of your importance to the continued success of the Company.

Your opportunity to earn a Recognition Bonus is subject to the terms and conditions contained in this Agreement.

I. Recognition Bonus

1. Subject to the terms and conditions described below, you will be eligible to receive a bonus equal to $163,000.00 (the "Recognition Bonus").

2. The Recognition Bonus will be payable, in cash, in two equal installments, as follows: (a) fifty percent (50%) of the Recognition Bonus will be paid as soon as administratively feasible (but in no event later than thirty (30) days) following December 31, 2022, and (b) fifty percent (50%) of the Recognition Bonus will be paid as soon as administratively feasible (but in no event later than thirty (30) days) following March 31, 2023 (each of the payment events in subclauses (a) and (b), a "Payment Event"), in either case so long as you remain in active employment with the Company or its affiliates until the occurrence of the applicable Payment Event.

3. If your employment terminates for any reason prior to a Payment Event, it will be in the sole discretion of the Compensation Committee to determine whether you are eligible to receive any portion of the Recognition Bonus that has not already been paid, and unless otherwise determined by the Compensation Committee, you will have no entitlement to receive any such unpaid amounts.

4. The Recognition Bonus is subject to all applicable tax withholding requirements, as determined by the Company.

II. Definitions

For purposes of this Agreement, the following terms shall have the following meanings:

1. "Board" means the board of directors of the Company.

2. "Compensation Committee" means the compensation committee of the Board.

III. Assignment

This Agreement is personal to you and may not be assigned by you other than by will or the laws of descent and distribution. This Agreement shall inure to the benefit of, and be enforceable against the Company by, your legal representatives, executors, administrators, successors, heirs, distributes or legatees.

This Agreement shall inure to the benefit of and be binding upon the Company and its successors. The Company shall require any successor to all or substantially all of the business and/or assets of the Company or any division of the Company, whether direct or indirect, by purchase, merger, consolidation, acquisition of stock, or otherwise, to expressly assume and agree to perform this Agreement in the same manner and to the same extent as the Company would be required to perform it if no such succession had taken place. Following such a change in control transaction, references in this Agreement to the Company shall mean the Company or the successor to the business and/or assets of the Company or any division of the Company, as the case may be.

IV. Parachute Payments

If any of the payments or benefits provided or to be provided by the Company or its affiliates to you or for your benefit pursuant to this Agreement or otherwise ("Covered Payments") constitute parachute payments within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code") and would, but for this paragraph, be subject to the excise tax imposed under Section 4999 of the Code (or any successor provision thereto) or any similar tax imposed by state or local law or any interest or penalties with respect to such taxes (collectively, the "Excise Tax"), then the Covered Payments shall be payable either (a) in full or (b) reduced to the minimum extent necessary to ensure that no portion of the Covered Payments is subject to the Excise Tax, whichever of the foregoing (a) or (b) results in your receipt on an after-tax basis of the greatest amount of benefits after taking into account the applicable federal, state, local and foreign income, employment and excise taxes (including the Excise Tax).

V. No Employment Rights

Neither this Agreement nor the grant of the Recognition Bonus creates a guarantee of continued employment for any period or a limitation on the Company's or any of its affiliates' right to terminate your employment at any time.

VI. Section 409A

This Agreement shall be interpreted to avoid any penalty or sanction under Section 409A of the Code ("Section 409A"). Any payments to you pursuant to this Agreement are intended to be exempt from Section 409A as short-term deferral pursuant to Treasury Regulation §1.409A-1(b)(4) or under such other exemption(s) as may apply. Notwithstanding the foregoing, the Company makes no representations that the payments provided under this Agreement comply with Section 409A and in no event shall the Company be liable for all or any portion of any taxes, penalties, interest or other expenses that may be incurred by you on account of non-compliance with Section 409A.

VII. Governing Law

This Agreement shall be governed by and construed in accordance with the law of the Commonwealth of Massachusetts without reference to principles of conflict of laws.

VIII. Counterparts

This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which taken together shall constitute one and the same instrument.

IX. Amendment

No amendment of this Agreement shall be valid unless made in writing and signed by both parties hereto.

X. Entire Agreement

This Agreement contains the entire understanding of the parties and supersedes any prior understanding and agreements between them representing the subject matter hereof, including but not limited to the prior retention bonus letter agreement, dated October 3, 2022, between you and the Company

[Signature page follows]

Please indicate your acceptance of this Agreement by signing on the appropriate space below and returning a signed copy to the Company.

Very truly yours,

CYCLERION THERAPEUTICS, INC.

By: /s/ Peter Hecht
Name: Peter Hecht
Title: CEO

ACCEPTANCE AND AGREEMENT:

I have read, understand, and agree to participate in and comply with the terms and conditions of the Agreement described above. This Agreement constitutes the full and complete understanding between me and the Company regarding the Recognition Bonus and may be amended only in writing signed by both parties.

/s/ Anjeza Gjino
Anjeza Gjino

Date: December 21, 2022

Cyclerion Therapeutics, Inc.

December 21, 2022
Cheryl Gault

Re: Amended and Restated Recognition Bonus Agreement

Dear Cheryl:

This letter agreement (this "Agreement") between you and Cyclerion Therapeutics, Inc. (the "Company") amends and restates the prior retention bonus letter agreement, dated October 3, 2022, between you and the Company, with respect to your opportunity to earn a Recognition Bonus (as defined below). The Company is offering you this opportunity in recognition of your importance to the continued success of the Company.

Your opportunity to earn a Recognition Bonus is subject to the terms and conditions contained in this Agreement.

I. Recognition Bonus

1. Subject to the terms and conditions described below, you will be eligible to receive a bonus equal to $171,000.00 (the "Recognition Bonus").

2. The Recognition Bonus will be payable, in cash, in two equal installments, as follows: (a) fifty percent (50%) of the Recognition Bonus will be paid as soon as administratively feasible (but in no event later than thirty (30) days) following December 31, 2022, and (b) fifty percent (50%) of the Recognition Bonus will be paid as soon as administratively feasible (but in no event later than thirty (30) days) following March 31, 2023 (each of the payment events in subclauses (a) and (b), a "Payment Event"), in either case so long as you remain in active employment with the Company or its affiliates until the occurrence of the applicable Payment Event.

3. If your employment terminates for any reason prior to a Payment Event, it will be in the sole discretion of the Compensation Committee to determine whether you are eligible to receive any portion of the Recognition Bonus that has not already been paid, and unless otherwise determined by the Compensation Committee, you will have no entitlement to receive any such unpaid amounts.

4. The Recognition Bonus is subject to all applicable tax withholding requirements, as determined by the Company.

II. Definitions

For purposes of this Agreement, the following terms shall have the following meanings:

1. "Board" means the board of directors of the Company.

2. "Compensation Committee" means the compensation committee of the Board.

III. Assignment

This Agreement is personal to you and may not be assigned by you other than by will or the laws of descent and distribution. This Agreement shall inure to the benefit of, and be enforceable against the Company by, your legal representatives, executors, administrators, successors, heirs, distributes or legatees.

This Agreement shall inure to the benefit of and be binding upon the Company and its successors. The Company shall require any successor to all or substantially all of the business and/or assets of the Company or any division of the Company, whether direct or indirect, by purchase, merger, consolidation, acquisition of stock, or otherwise, to expressly assume and agree to perform this Agreement in the same manner and to the same extent as the Company would be required to perform it if no such succession had taken place. Following such a change in control transaction, references in this Agreement to the Company shall mean the Company or the successor to the business and/or assets of the Company or any division of the Company, as the case may be.

IV. Parachute Payments

If any of the payments or benefits provided or to be provided by the Company or its affiliates to you or for your benefit pursuant to this Agreement or otherwise ("Covered Payments") constitute parachute payments within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code") and would, but for this paragraph, be subject to the excise tax imposed under Section 4999 of the Code (or any successor provision thereto) or any similar tax imposed by state or local law or any interest or penalties with respect to such taxes (collectively, the "Excise Tax"), then the Covered Payments shall be payable either (a) in full or (b) reduced to the minimum extent necessary to ensure that no portion of the Covered Payments is subject to the Excise Tax, whichever of the foregoing (a) or (b) results in your receipt on an after-tax basis of the greatest amount of benefits after taking into account the applicable federal, state, local and foreign income, employment and excise taxes (including the Excise Tax).

V. No Employment Rights

Neither this Agreement nor the grant of the Recognition Bonus creates a guarantee of continued employment for any period or a limitation on the Company's or any of its affiliates' right to terminate your employment at any time.

VI. Section 409A

This Agreement shall be interpreted to avoid any penalty or sanction under Section 409A of the Code ("Section 409A"). Any payments to you pursuant to this Agreement are intended to be exempt from Section 409A as short-term deferral pursuant to Treasury Regulation §1.409A-1(b)(4) or under such other exemption(s) as may apply. Notwithstanding the foregoing, the Company makes no representations that the payments provided under this Agreement comply with Section 409A and in no event shall the Company be liable for all or any portion of any taxes, penalties, interest or other expenses that may be incurred by you on account of non-compliance with Section 409A.

VII. Governing Law

This Agreement shall be governed by and construed in accordance with the law of the Commonwealth of Massachusetts without reference to principles of conflict of laws.

VIII. Counterparts

This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which taken together shall constitute one and the same instrument.

IX. Amendment

No amendment of this Agreement shall be valid unless made in writing and signed by both parties hereto.

X. Entire Agreement

This Agreement contains the entire understanding of the parties and supersedes any prior understanding and agreements between them representing the subject matter hereof, including but not limited to the prior retention bonus letter agreement, dated October 3, 2022, between you and the Company

[Signature page follows]

Please indicate your acceptance of this Agreement by signing on the appropriate space below and returning a signed copy to the Company.

Very truly yours,

CYCLERION THERAPEUTICS, INC.

By: /s/ Peter Hecht
Name: Peter Hecht
Title: CEO

ACCEPTANCE AND AGREEMENT:

I have read, understand, and agree to participate in and comply with the terms and conditions of the Agreement described above. This Agreement constitutes the full and complete understanding between me and the Company regarding the Recognition Bonus and may be amended only in writing signed by both parties.

/s/ Cheryl Gault
Cheryl Gault

Date: December 21, 2022

Exhibit 21.1

List of Registrant's Subsidiaries

Cyclerion Securities Corporation, incorporated in Massachusetts, a wholly owned subsidiary.

Cyclerion GmbH, incorporated in Switzerland, a wholly owned subsidiary.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-257145) of Cyclerion Therapeutics, Inc. and the related Prospectus,

(2) Registration Statement (Form S-3 No. 333-240095) of Cyclerion Therapeutics, Inc. and the related Prospectus,

(3) Registration Statement (Form S-3 No. 333-242334) of Cyclerion Therapeutics, Inc. and the related Prospectus,

(4) Registration Statement (Form S-8 No. 333-248957) pertaining to 2019 Equity Incentive Plan, 2019 Employee Stock Purchase of Cyclerion Therapeutics, Inc.,

(5) Registration Statement (Form S-8 No. 333-258316) pertaining to 2019 Equity Incentive Plan, 2019 Employee Stock Purchase of Cyclerion Therapeutics, Inc.,

(6) Registration Statement (Form S-8 No. 333-230615) pertaining to 2019 Equity Incentive Plan, 2019 Employee Stock Purchase Plan, Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan, and Amended and Restated 2005 Stock Incentive Plan of Cyclerion Therapeutics, Inc.;

of our report dated March 22,2023, with respect to the consolidated financial statements of
Cyclerion Therapeutics, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 22, 2023

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Peter M. Hecht, certify that:

1. I have reviewed this annual report on Form 10-K of Cyclerion Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 22, 2023

By: /s/ Peter Hecht
Name: Peter M. Hecht
Title: Chief Executive Officer (Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Anjeza Gjino, certify that:

1. I have reviewed this annual report on Form 10-K of Cyclerion Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13-a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 22, 2023

By: /s/ Anjeza Gjino
Name: Anjeza Gjino
Title: Chief Financial Officer (Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Peter M. Hecht, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Annual Report on Form 10-K of Cyclerion Therapeutics, Inc. for the period ended December 31, 2022 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-K fairly presents, in all material respects, the financial condition and results of operations of Cyclerion Therapeutics, Inc.

Date: March 22, 2023

By: /s/ Peter Hecht
Name: Peter M. Hecht
Title: Chief Executive Officer (Principal Executive Officer)

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Anjeza Gjino, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Annual Report on Form 10-K of Cyclerion Therapeutics, Inc. for the period ended December 31, 2022 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-K fairly presents, in all material respects, the financial condition and results of operations of Cyclerion Therapeutics, Inc.

Date: March 22, 2023

By: /s/ Anjeza Gjino

Name: Anjeza Gjino

Title: Chief Financial Officer (Principal Financial and Accounting Officer)