Risk Factors Comparison 2025-03-04 to 2024-03-05 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

• 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 current and any potential future 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~~ **We are in the process of in- licensing a product candidate for treatment resistant depression and our** approach to the discovery and development of ~~our~~ **this and any future** product candidates **we may develop** may never lead to marketable products. **Risks Related to Development and Clinical Testing of Our Products and Product Candidates** • 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. • We could encounter difficulties in enrolling participants in ~~our~~ **any future** clinical studies, which could delay or prevent progress of our product candidates. • We may be unable to obtain regulatory approval **f** ~~for our product candidates~~ and unable to generate product revenue **for any product candidate** . • ~~Our~~ **Any future** 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. **Risks Related to Reliance on Licensees, Tisento and Third Parties** • ~~We may not succeed in our pursuit of capital, capabilities, and transactions for the development and commercialization of our assets. • The~~ **There are** risks in our investment in Tisento tied to Tisento developing, obtaining regulatory approval for, launching and commercializing ~~their~~ **its** product candidates. • ~~The~~ **There is** uncertainty as to any liquidity or monetizable value of our equity interest in Tisento, which faces all the risks of an early- stage pharmaceutical development company. • Akebia may not be successful in developing and commercializing any therapies through ~~the~~ **its** praliciguat out- license with the Company. • We **may not be successful in entering into necessary licenses or collaboration agreements and 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. **Risks Related to Intellectual Property** • 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. **Risks Related to the Future Commercialization of our Potential Future Product Candidates** • 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 **, as well as the potential for reductions in federal government funding for development and clinical trials** may harm our business. • Our prospects for success depend on our ability to attract, retain and motivate qualified personnel. • We ~~may~~ **will** 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. • If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to, regulatory investigations or actions; litigation; fines and penalties; interruptions to our commercial operations, clinical trials or other operations; harm to our reputation; loss of revenue or profits; loss of sales and other adverse consequences. • 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 **. • The pandemic and future pandemics may disrupt our business, including our development activities. Risks Related to the holders of Our Common Stock • We have limited trading history and a relatively limited public float for our shares and our common stock market price may fluctuate widely. • 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** . • Any future failure to comply 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 ~~. • The COVID- 19 pandemic and future pandemics may disrupt our business, including our development activities~~ . 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 which occurred in 2019. We are **seeking to** ~~developing~~ --- **develop new products for treatment resistant depression. We have also developed** a pipeline of sGC stimulators, but we have no products approved for commercial sale, and we have never generated revenue from product sales **nor have Tisento or Akebia ever generated product sales from products incorporating our compounds** . 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, **2024 and** 2023 ~~and 2022~~ were $ **3. 1 million and $** 5. 3 ~~million and $ 44. 1~~ million, respectively. We expect to incur significant losses for at least **the next** 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 current and any potential future 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 **in the near term** , 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, ~~2023~~ **2024** , we had unrestricted cash and cash equivalents of approximately $ ~~7~~ **3** . ~~6~~ **2** million. Our management believes that such cash and cash equivalents will not be sufficient to fund our operating expenses and capital requirements **beyond** ~~for one year after~~ the **second quarter** ~~date the financial statements are issued~~ , whether or not we curtail efforts with respect to certain of our current and future 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 ~~intend to seek funds through collaborations, strategic alliances, or licensing arrangements with third parties. Such agreements may adversely impact retained rights to our assets, technologies, future revenue streams and programs, especially those that receive regulatory approval. We~~ may also seek to raise such capital through public or private ~~equity~~ **financing of our securities** , 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 **. If we sell shares or other equity securities in one or more other transactions, or issue stock, stock options or other securities pursuant to our current equity plans, investors may be materially diluted by such subsequent issuances. We will need significant additional capital in the near term to continue our current plans. No assurance can be given that we will be able to obtain such funds upon favorable terms and conditions, if at all. Failure to do so could have a material adverse effect on our business. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, preferred stock, convertible securities or other equity or convertible securities in one or more transactions that may include voting rights (including the right to vote as a series on particular matters), preferences as to dividends and liquidation, antidilution, and conversion and redemption rights, subject to applicable law, and at prices and in a manner we determine from time to time. Such issuances and the exercise of any convertible securities will dilute the percentage ownership of our stockholders and may affect the value of our capital stock and could adversely affect the rights of the holders of such stock, thereby reducing the value of such stock. Moreover, any exercise of convertible securities may adversely affect the terms upon which we will be able to obtain additional equity capital, since the holders**

of such convertible securities can be expected to exercise them at a time when we would, in all likelihood, not be able to obtain any needed capital on terms more favorable to us than those provided in such convertible securities . 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~~ **In the event we are unable** to **raise financing, we may need to reduce** ~~our~~ **or** ~~Business~~ **cease operations. We also intend to seek funds through collaborations, strategic alliances, or licensing arrangements with third parties. Such agreements may adversely impact retained rights to our assets, technologies, future revenue streams** and ~~Industry~~ **programs, especially those that receive regulatory approval.** Our approach to the discovery and development of product candidates for the treatment of serious diseases may never lead to marketable products. The development of drug therapies presents unique challenges ~~.~~, including an imperfect understanding of the biology, 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 current and any potential future product candidates. The scientific evidence to support the feasibility of developing our current 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 products to treat patients with serious diseases. Our business depends heavily on the successful development, clinical testing, regulatory approvals and commercialization of olinciguat **(optioned to CVCO)** and praliciguat (out- licensed to Akebia), ~~our retained systemic sGC stimulators~~ and any future potential product candidates we may acquire or license as well as both the Transferred Assets product candidates we have sold to Tisento. Any of our current or potential product candidates will require regulatory approval. 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. 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 ~~as well as the product candidates we have out- licensed to Akebia and the Transferred Assets sold to Tisento~~ . The timing of any clinical studies will depend in part on the speed at which participants can be recruited to participate in testing these 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, Akebia and any other future licensees, as applicable, are ultimately unable to obtain regulatory approval for the 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 we own, licensed to Akebia or sold to

Tisento has been requested or obtained, and it is possible that none of these existing product candidates or any product candidates we or our licensees or Tisento 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, our licensees or Tisento 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; **• cutbacks in funding for the FDA may result in delays in reviewing and approving applications;** 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, Tisento, 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. Our current and any potential future product candidates ~~, those licensed to Akebia and those sold to Tisento~~ may cause serious side effects which could cause us, our licensees, Tisento, 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 nonclinical studies and clinical studies of our product candidates ~~, those licensed to Akebia and those sold to Tisento 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 for those product candidates we retain our out- license or to realize value in our equity position in Tisento. Obtaining and maintaining regulatory approval of 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 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 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, our licensees or Tisento 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 these product candidates is subsequently approved. If these 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. ~~The COVID- 19 pandemic and other future~~ **Future** pandemics may disrupt our business, including our development activities. Many nations, including the United States, continue to implement mitigation measures ~~,~~ that have in the past and may in the future limit our ability to access patients and physicians at certain local clinical centers that are participating in any future development activities. We may face limitations and difficulties enrolling patients in our planned and future clinical trials if the patient populations that are eligible for our clinical trials are affected by the coronavirus and / or the COVID- 19 vaccines or other pandemics. Any such restrictions at trial sites could delay any future clinical studies. In addition, if the patients enrolled in any future clinical trials become infected with COVID- 19 or other viruses, we may have more adverse events and deaths in our clinical trials as a result. Vulnerable patients may be at a higher risk of contracting COVID- 19 and other viruses 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 vaccines to patients participating in our future clinical trials could adversely affect clinical trial outcomes or data analysis. Furthermore, the extent to which the COVID- 19 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 COVID- 19 pandemic, or future outbreaks of infectious disease, may increase our capital needs while potentially interfering with our access to capital. Risks Related to ~~Our~~ Reliance on **Licensees, Tisento and Other** Third Parties We may not succeed in our pursuit of capital, capabilities, and transactions for the development and commercialization of our future clinical stage assets, which would affect our financial condition. We **are seeking** ~~intend in the future to seek~~ capital, capabilities, and transactions to advance the development of product candidates we may acquire rights to in the future. 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. **On December 13, 2024, we and Akebia entered into Amendment # 1 to License Agreement (the " 2024 Amendment ") to the original 2021 license agreement. Under the terms of the 2024 Amendment, Akebia paid the Company (i) $ 1. 25 million in December 2024 and has agreed to pay an additional $ 0. 5 million on or before September 30, 2025. In addition, Akebia has agreed to assume control of the preparation, filing, prosecution and maintenance of certain** Cyclerion **patents, and** ~~is eligible to receive up to $ 12 million upon~~ the ~~initiation of a phase 2 clinical trial~~ **expenses associated therewith, at an earlier date than as originally agreed between the parties** . ~~Cyclerion is eligible~~ **The parties have agreed** to **the reduction of certain** ~~receive up to $ 585 million in total potential future~~ development ~~, regulatory, and commercialization milestone~~ **milestones** ~~payments~~ **and the increase of certain royalty rates on net sales and sublicense income** . **Pursuant to the terms of the 2021 License Agreement, as amended,** Akebia will pay Cyclerion tiered ~~royalty~~ **royalties** ~~payments on net sales in certain major markets at percentages~~ ranging from ~~the~~ mid- single ~~digits~~ - **digit** to ~~the high- teens, subject~~ **twenty percent of net sales. Cyclerion' s obligations** to **deliver** certain ~~reductions and offsets~~ **drug products have also ceased** . The agreement may be terminated by either party in the event of a material breach by the other party or by us in the event of certain patent disputes. 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 or that Akebia will be able to successfully bring any of the licensed product candidates to market due to financial limitations or other business factors in the future or if Akebia is unable to raise additional capital on favorable terms, if at all. Akebia may at any time terminate the Akebia License Agreement upon 180 days written notice. subject to Akebia' s obligation to grant Cyclerion a non- exclusive, royalty- free license, with the right to grant multiple tiers of sublicenses, to certain licensed compounds or products as defined in the Akebia License Agreement as well as certain rights to regulatory submissions, product trademarks, contracts with third party suppliers and certain other rights. Tisento may not be successful in developing any therapies and we may not realize any future value from the Tisento common stock we received under the Asset Purchase Agreement with Tisento. Our investment in Tisento is subject to all of the risks associated with an earlier stage biotechnology company. The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that Tisento' s technology,

development experience and scientific knowledge provide it with competitive advantages, it may face potential competition from many different sources, including large pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for the research, development, manufacturing and commercialization of similar products. Any investigational products that we successfully develop and commercialize will compete with new immunotherapies that may become available in the future. As a result, our investment in Tisento is risky and our equity interest in Tisento could be significantly diluted in the future if Tisento seeks to raise additional capital or is unable to raise additional capital on favorable terms, if at all. If Tisento suffers adverse effects, it may not be able to continue as a going business concern, and we may lose our entire investment. We lack operational control over Tisento. Our investment in Tisento represents a minority or passive stake and we may have little to no participation, input or control over the management, policies, and operations of Tisento. Further, we may lack sufficient ownership of voting securities to impact, without the vote of additional equity holders, any matters submitted to stockholders or members of such business for a vote. There is inherent risk in making minority equity investments in companies over which we have little to no control. Without control of the management and decision- making of these businesses, we cannot control their direction, strategy, policies and business plans, and we may be powerless to improve any declines in their performance, operating results and financial condition. 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 any potential 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 expect in the future to rely on third parties to conduct any nonclinical or clinical studies for any potential future 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 any potential future 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 expect to rely on contract laboratories, medical institutions, clinical investigators, licensees and other third parties, such as CROs, to conduct nonclinical studies on any future discovery compounds and product candidates and clinical studies on product candidates. We expect to rely heavily on such parties for execution of nonclinical and clinical studies and as a result that we will only be able to control certain aspects of their activities. As a result, we expect we will 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 any future 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, and any future 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 potential future nonclinical studies, clinical studies or product manufacturing will comply 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 current licensee or any future 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 current or any potential 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 expect to depend on third- party contract manufacturing organizations, or CMOs, for all our requirements of raw materials, drug substances and drug product for any future nonclinical studies and clinical trials. We do not have long- term supply agreements in place with any CMO and we expect that any potential future product candidates will be individually contracted under a services agreement on a purchase order basis. We expect 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 any 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 expect in the future to 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, any facilities which may be used by 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 anticipated 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 seek to involve third party licensees and collaborators on current and potential future product candidates, we expect we will rely on third parties to manufacture our product candidates, and because we expect to 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 or Tisento are unable to adequately protect proprietary technologies, or obtain and maintain issued patents that are sufficient to protect ~~our~~ **their respective** product candidates, others could compete against us, our licensees and Tisento more directly, which would have a material adverse impact on our business, prospects, financial condition and results of operations. Our success will depend in part on our and our licensees and Tisento' s 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 ~~nineteen~~ **20** issued U. S. patents, ~~nine~~ **eleven** pending U. S. patents applications and numerous foreign patents and pending patent applications. Patent families are filed either as utility ~~US~~ **U. S.** patents or under an

international patent law treaty (PCT) that provides a unified procedure for filing a single initial patent application to seek patent protection for an invention simultaneously in each of the 157 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 **or other** ~~court~~ **courts** . 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 attorneys' 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. Our employee, 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 and Tisento 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 involves 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. Our current employee and any employees we may hire in the future may have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage and, in the future, intend to 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 Current or Potential Future Product Candidates The incidence and prevalence for target patient populations of our current and any potential future product candidates we may acquire have not been established with precision. If the market opportunities for our current and potential future 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 current and any potential future 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 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 **and cost- cutting measures at the federal and state level currently proposed for Medicaid and other programs** . 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 PTC Therapeutics, Travere Therapeutics, Dimerix Limited, Vertex Pharmaceuticals, Chinook Therapeutics, Boehringer Ingelheim, River 3 Renal Corp, Astellas, Pfizer, Eli Lilly, Novartis, AstraZeneca, Bayer and Merck are our most direct competitors with respect to 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, as well as the Inflation Reduction Act of 2022 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 and in reducing the costs of certain prescription drugs as evidenced by the Inflation Reduction Act of 2022. 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 any current and potential future 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 current and any potential future 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 Regina Graul, our President and **Chief Executive Officer and** in the future to attract, retain and motivate qualified personnel. We are highly dependent on Regina Graul, Ph. D. who is currently our sole employee. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Our success also depends on our ability ~~to~~ in the future **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. The use of our current and any potential future 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 such 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 potential 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. **As** ~~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, **we are** ~~which would allow us to take advantage of many of the same exemptions from disclosure requirements, including exemption~~ --- **exempt** 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 **a** ~~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, ~~2023~~ **2024** , 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, which status will end on December 31, 2024 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 **and political** 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 **as well as adverse economic conditions caused by political unrest** . A severe or prolonged economic downturn **and severe political disruption** 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 **. If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to, regulatory investigations or actions; litigation; fines and penalties; interruptions to our commercial operations, clinical trials or other operations; harm to our reputation; loss of revenue or profits; loss of sales and other adverse consequences** . In the ordinary course of our business, we and our third- party service providers may process proprietary, confidential, and sensitive data, including personal data (such as health- related data and data related to our clinical trials), intellectual property, and trade secrets (collectively, sensitive information). Cyberattacks, malicious internet- based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources, including traditional computer " hackers, " threat actors, personnel (such as through theft or misuse)," hacktivists", organized criminal threat actors, sophisticated nation- states, and nation- state- supported actors. Some actors now engage and are expected to continue to engage in cyberattacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyberattacks that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our products. We and the third parties upon which we rely may be subject to a variety of other evolving threats, including, but not limited to, social- engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, attacks enhanced or facilitated by artificial intelligence, and other similar threats. In particular, ransomware attacks, including those from organized criminal threat actors, nation- states and nation- state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, ability to provide our products, disruption of clinical trials, loss of data (including data related to clinical trials), loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the financial, operational and reputational impact of a ransomware attack, it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws prohibit such payments). Additionally, hybrid and remote work has become more common and has increased risks to our

information technology systems and data, as more of our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit, and in public locations. Future or past business transactions (such as acquisitions or integrations) could also expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We rely upon third parties and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, third- party providers of cloud- based infrastructure, encryption and authentication technology, employee email, and other functions. We also rely on third parties to provide certain products, including active pharmaceutical ingredients, to operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. While we may be entitled to damages if the third parties upon which we rely fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. We may share or receive sensitive information with or from third parties. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate and remediate vulnerabilities in our information security systems (such as our hardware and / or software, including that of third parties upon which we rely), but we may not be able to detect, mitigate, and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our products. We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations require us to implement and maintain specific security measures, industry- standard or reasonable security measures to protect our information technology systems and sensitive information. Applicable data security and public company disclosure obligations may require us to notify relevant stakeholders of certain security incidents, including affected individuals, customers, regulators and investors. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and / or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; diversion of management attention; interruptions in our operations (including availability of data); financial loss and other similar harms. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Whether a cybersecurity incident is reportable to our investors may not be straightforward, may take considerable time to determine, and may be subject to change as the investigation of the incident progresses, including changes that may significantly alter any initial disclosure that we provide. Moreover, experiencing a material cybersecurity incident and any mandatory disclosures could lead to negative publicity, loss of customer, investor or partner confidence in the effectiveness of our cybersecurity measures, diversion of management' s attention, governmental investigations, lawsuits, and the expenditure of significant capital and other resources. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. In addition, our insurance coverage may not be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices or that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Sensitive information of us or our customers could also be leaked, disclosed, or revealed as a result of or in connection with our employee' s, personnel' s, or vendor' s use of generative AI technologies. Our employee or future 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 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 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 ". We effected a 20: 1 reverse stock split in May 2023. As a result, we have regained compliance with the Bid Price Requirement. If the Company does not regain compliance with the Bid Price Requirement in the future, the Company' s stock will again be subject to delisting. **As a result of amendments in October 2024 to the NASDAQ delisting procedures, NASDAQ now may automatically delist companies which conduct multiple reverse stock splits in any 12- month period.** 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 maintain 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~~ **for** 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: • **failure to raise additional capital on a timely basis and the terms on which we raise any capital; •** a relatively low **public float** ~~- 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, those out- licensed to third parties and the Transferred Assets sold to Tisento, 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. We run the risk of inadvertently being deemed an investment company required to register under the Investment Company Act of 1940. We run the risk of inadvertently being deemed an investment company required to register under the Investment Company Act of 1940 (the " Investment Company Act ") because a significant portion of our assets consists of investments in companies in which we own less than a majority interest. The risk varies depending on events beyond our control, such as significant appreciation or depreciation in the market value of certain of our publicly traded holdings, adverse developments with respect to our ownership of certain of our subsidiaries, transactions involving the sale of certain assets and our participation in any partnership or other fund established to finance future broadband and real estate projects in which we may engage. If we are deemed to be an inadvertent investment company, we may seek to rely on a safe harbor under the Investment Company Act that would provide us a one- year grace period to take steps to avoid being deemed to be an investment company. In order to ensure we avoid being deemed an investment company, we have taken, and may need to continue to take, steps to reduce the percentage of our assets that constitute investment assets under the Investment Company Act. These steps have included, among others, selling marketable securities that we might otherwise hold for the long term and deploying our cash in non- investment assets. We have recently sold marketable securities, including at times at a loss, and we may be forced to sell our investment assets at unattractive prices or to sell assets that we otherwise believe benefit our business in the future to remain below the requisite threshold. We may also seek to acquire additional non- investment assets to maintain compliance with the Investment Company Act, and we may need to incur debt, issue additional equity or enter into other financing arrangements that are not otherwise attractive to our business. Any of these actions could have a material adverse effect on our results of operations and financial condition. Moreover, we can make no assurance that we would successfully be able to take the necessary steps to avoid being deemed to be an investment company in accordance with the safe harbor. If we were unsuccessful, then we would have to register as an investment company, and we would be unable to operate our business in its current form. We would be subject to extensive, restrictive, and potentially adverse statutory provisions and regulations relating to, among other things, operating methods, management, capital structure, indebtedness, dividends, and transactions with affiliates. If we were deemed to be an investment company and did not register as an investment company when required to do so, there would be a risk, among other material adverse consequences, that we could become subject to monetary penalties or injunctive relief, or both, that we would be unable to enforce contracts with third parties, and / or that third parties could seek to obtain rescission of transactions with us undertaken during the period in which we were an unregistered investment company. Uncertainties in the interpretation and application of existing, new and proposed tax laws and regulations could materially affect our tax obligations and effective tax rate. The tax regimes to which we are subject or under which we operate are unsettled and may be subject to significant change. The issuance of additional guidance related to existing or future tax laws, or changes to tax laws or regulations proposed or implemented by the current or a future U. S. presidential administration, Congress, or taxing authorities in other jurisdictions, including jurisdictions outside of the United States, could materially affect our tax obligations and effective tax rate. To the extent that such changes have a negative impact on us, including as a result of related uncertainty, these changes may adversely impact our business, financial condition, results of operations, and cash flows. The amount of taxes we pay in different jurisdictions depends on the application of the tax laws of various jurisdictions, including the United States, to our international business activities, tax rates, new or revised tax laws, or interpretations of tax laws and policies, and our ability to operate our business in a manner consistent with our corporate structure and intercompany arrangements. The taxing authorities of the jurisdictions in which we operate may challenge our methodologies for pricing intercompany transactions pursuant to our intercompany arrangements or disagree with our determinations as to the income and expenses attributable to specific jurisdictions. If such a challenge or disagreement were to occur, and our position was not sustained, we could be required to pay additional taxes, interest, and penalties, which could result in one- time tax charges, higher effective tax rates, reduced cash flows, and lower overall profitability of our operations. Our financial statements could fail to reflect adequate reserves to cover such a contingency. Similarly, a taxing authority could assert that we are subject to tax in a jurisdiction where

we believe we have not established a taxable connection, often referred to as a " permanent establishment " under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. Effective January 1, 2022, the Tax Cuts and Jobs Act of 2017 eliminated the option to deduct research and development expenses for tax purposes in the year incurred and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over 15 years of research activities conducted outside the United States. Unless the United States Department of the Treasury issues regulations that narrow the application of this provision to a smaller subset of our research and development expenses or the provision is deferred, modified, or repealed by Congress, in future years we may experience a material decrease in our cash flows from operations and an offsetting similarly sized increase in our net deferred tax assets over these amortization periods. The actual impact of this provision will depend on multiple factors, including the amount of research and development expenses we will incur and whether we conduct our research and development activities inside or outside the United States and our overall net operating loss position. Our ability to use net operating loss carryforwards and certain other tax attributes to offset future taxable income and taxes may be subject to limitations. Under current law, our federal net operating losses (" NOLs") generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80 % of taxable income. As of December 31, ~~2023~~ **2024** , we had federal NOLs of $ ~~177~~ **195** million. It is uncertain if and to what extent various states will conform to federal tax laws. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is generally defined as a greater than 50 % change, by value, in its equity ownership over a three- year period, the corporation' s ability to use its pre- change NOL carryforwards and other pre- change U. S. tax attributes (such as research tax credits) to offset its post- change income or taxes may be limited. ~~We are in the process of updating our analysis of owner shifts to determine whether an ownership change occurred since March 30, 2019.~~ It is possible that we have experienced an ownership change in the past. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control **, as well as the issuance of additional securities if we are successful in raising equity capital** . As a result, our federal NOL carryforwards may be subject to a percentage limitation if used to offset income in tax years following an ownership change. In addition, it is possible that we have in the past undergone, and in the future may undergo, additional ownership changes that could limit our ability to use all of our pre- change NOL carryforwards and other pre- change tax attributes (such as research tax credits) to offset our post- change income or taxes. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOL carryforwards and other tax attributes, which would harm our future operating results by effectively increasing our future tax obligations. We maintain our cash at financial institutions, often in balances that exceed federally insured limits. We maintain the majority of our cash and cash equivalents in accounts at banking institutions in the United States that we believe are of high quality. Cash held in these accounts often exceeds the FDIC insurance limits. If such banking institutions were to fail, we could lose all or a portion of amounts held in excess of such insurance limitations. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. 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. **Currently, no industry analysts cover our stock.** 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 have never paid cash dividends and 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.