**Risk Factors Comparison 2024-03-28 to 2023-03-08 Form: 10-K**

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

~~• Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our consolidated financial statements and the related notes and " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could adversely affect our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Risks Related to Our Financial Position and Capital Needs~~ We are a ~~clinical stage~~ biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future. ~~•~~ We have ~~incurred losses in each year since our inception in 2012 and anticipate incurring losses for the foreseeable future. To date, we have invested substantially all of our efforts and financial resources in identifying, acquiring, in- licensing and developing our product candidates, including commencing and conducting clinical trials and providing general and administrative support for these operations. Our future success is dependent on our ability to develop, obtain regulatory approval for and successfully commercialize one or more of our product candidates. We have not yet demonstrated our ability to obtain regulatory approvals, manufacture a drug at commercial scale, or conduct sales and marketing activities. We~~ currently **halted** ~~generate no revenue from sales of any products, and we may never be able to develop or commercialize a marketable product. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Typically, it takes many years to develop one new drug from the time it is discovered to when it is available for treating patients, and development may cease for a number of reasons. We have incurred significant losses related to expenses for research and development and our ongoing operations. Our net losses for the years ended December 31, 2022 and 2021 were $ 62. 2 million and $ 80. 5 million, respectively. As of December 31, 2022, we had an accumulated deficit of $ 378. 3 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we: • continue our~~ clinical development of our product candidates ~~; • advance our programs into more expensive clinical trials; • advance our ongoing research and preclinical development activities for our existing product candidates; • increase our manufacturing needs or add additional manufacturers or suppliers; • seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials~~ , ~~if any; • establish a sales, marketing~~ and ~~distribution infrastructure to commercialize any products for which we may obtain marketing approval; • seek to identify, assess, acquire or develop additional product candidates; • make royalty or other payments under any royalty or purchase agreements, including our Amended and Restated Purchase and Sale Agreement, or the Royalty Agreement, as amended, by and among us, Clarus IV Galera Royalty AIV, L. P., Clarus IV- A, L. P., Clarus IV- B, L. P., Clarus IV- C, L. P. and Clarus IV- D, L. P., or, collectively, Blackstone or Blackstone Life Sciences (formerly Clarus); • seek to maintain, protect and expand our intellectual property portfolio; • seek to attract and retain skilled personnel; • create additional infrastructure to support our product development and our planned future commercialization efforts; and • experience any delays or encounter issues with any of the above, including but not limited to failed trials, complex results, safety issues, other regulatory challenges that require longer follow- up of existing trials, additional major trials or additional supportive trials in order to pursue marketing approval. To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability. In cases where we are successful in obtaining regulatory approval to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Because of the numerous risks and uncertainties associated with product development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those expected, or if~~ there ~~are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase. Further, the net losses we incur may fluctuate significantly from quarter- to- quarter and year- to- year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. We expect to incur additional costs associated with operating as a public company. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern. We have incurred significant losses since our inception and have never generated revenue or profit, and it is possible we will never generate revenue or profit. As of~~

December 31, 2022, we had $ 31. 6 million in cash, cash equivalents and short- term investments and an accumulated deficit of $ 378. 3 million. Based on our current operating plan and assumptions, we believe that our existing cash, cash equivalents and short- term investments as of December 31, 2022, together with the net proceeds from our February 2023 registered direct offering, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2023, but not for more than one year after the date of the filing of this Annual Report on Form 10- K. These factors raise substantial doubt about our ability to continue as a going concern. We will need to raise additional capital to fund our future operations and remain as a going concern. There can be no assurance that we will **resume** be able to obtain additional funding on acceptable terms, if at all. To the extent that we raise additional capital through future equity offerings, the ownership interest of common stockholders will be diluted, which dilution may be significant. However, we cannot guarantee that we will be able to obtain any or sufficient additional funding or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that we are unable to obtain any or sufficient additional funding, there can be no assurance that we will be able to continue as a going concern, and we will be forced to delay, reduce or discontinue our product development programs or commercialization efforts. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock, and it may be more difficult for us to obtain financing. If potential collaborators decline to do business with us or potential investors decline to participate in any future financings due to such concerns, our ability to increase our cash position may be limited. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations. We have prepared our consolidated financial statements on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Our consolidated financial statements included in this Annual Report on Form 10- K do not include any adjustments to reflect the possible inability to continue as a going concern within one year after the date of the filing of this Annual Report on Form 10- K. If we are unable to continue as a going concern, you could lose all or part of your investment. We will need substantial funding to meet our financial obligations and to pursue our business objective. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy. Identifying potential product candidates and conducting preclinical studies and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. We expect our expenses to increase in connection with our ongoing development activities related to avasopasem for the reduction in the incidence of severe oral mucositis, or SOM, in patients with locally advanced HNC, seek marketing approval for avasopasem, pursue clinical trials and marketing approval of avasopasem in other indications, pursue clinical trials and marketing approval of rucosopasem and advance any of our other product candidates we may develop or otherwise acquire. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to manufacturing, product sales, marketing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed on attractive terms, if at all, we will be forced to delay, reduce or eliminate certain of our clinical development **in** plans, research and development programs or future commercialization efforts. The development process for our product candidates is highly uncertain, and we cannot estimate with certainty the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of our product candidates. Based on our current operating plan and assumptions, we believe that our existing cash, cash equivalents and short- term investments as of December 31, 2022, together with the net proceeds from our February 2023 registered direct offering, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2023. Our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than expected, through public or private equity, debt financings or other sources. Our future capital requirements will depend on and could increase significantly as a result of many factors, including: • the results, time and cost necessary for completing our ongoing and planned clinical trials; • the number, size and type of any additional clinical trials; • the costs, timing and outcomes of seeking and potentially obtaining approvals from the U. S. Food and Drug Administration, or FDA, or comparable foreign regulatory authorities, such as the European Commission, or the competent authorities of the member states of the European Union, or EU, including the potential for the FDA or comparable regulatory authorities to require that we conduct more studies and trials than those that we currently expect to conduct and the costs of post- marketing studies or risk evaluation and mitigation strategies, or REMS, or similar risk management measures that could be required by regulatory authorities; • the costs and timing of transferring manufacturing technology to third- party manufacturers, producing product candidates to support clinical trials and preparing to manufacture our product candidates; • our ability to successfully commercialize any of our product candidates, including the cost and timing of forming and expanding our sales organization and marketing capabilities; • the amount of sales revenues from our product candidates, if approved, including the sales price and the availability of coverage and adequate third- party reimbursement; • competitive and potentially competitive products and technologies and patients' receptivity to our product candidates and the technology underlying them in light of competitive products and technologies; • the cash requirements of any future acquisitions, developments or discovery of additional product candidates, including any licensing or collaboration agreements; • the time and cost necessary to respond to technological and market developments; • the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; • any product liability or other lawsuits related to our product candidates or any products; • the costs associated with being a public company; • our need and ability to hire additional personnel; and • the receptivity of the capital markets to financings by biotechnology companies generally and companies with product candidates and technologies such as ours specifically. Any additional fundraising efforts

may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our product candidates. Dislocations in the financial markets may make equity and debt financing more difficult to obtain and may have a material adverse effect on our - **or strategic** ability to meet our fundraising needs when they arise. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our preclinical studies, clinical trials or other research or development programs, the commercialization of any product candidate. We may also be unable to expand our operations ---- **option** or otherwise capitalize on our business opportunities or may be required to relinquish rights to our product candidates or products. Any of these occurrences could materially affect our business, financial condition and results of operations. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time as we **pursue** can generate substantial product revenues, if ever, we expect to finance our cash needs through securities offerings or debt financings, or possibly, license and collaboration agreements or research grants. The terms of any financing may **not** adversely affect the holdings or the rights of our stockholders and our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline. The sale of additional equity or convertible securities would dilute all of our stockholders, including your ownership interest. The incurrence of indebtedness would result in increased fixed or variable payment obligations, and we may be **successful** required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business . **•** We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies, product candidates or future revenue streams, or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. If we raise funds through research grants, we may be subject to certain requirements, which may limit our ability to use the funds or require us to share information from our research and development. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our stockholders and may cause the market price of our shares to decline. Risks Related to the Discovery and Development of Our Product Candidates We are heavily dependent on the success of our lead product candidate, avasopasem , **manganese (avasopasem)** and **, because avasopasem has not received regulatory approval and we have halted all commercial preparation efforts, our business has and may continue to be harmed. • The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations. • We rely, and will continue to rely, on third parties to conduct our clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. • If we are unable to establish our own sales, marketing and distribution capabilities, or enter into agreements with third parties to sell and market avasopasem or any other product candidates, we may not be successful in commercializing our product candidates** if **and when they** avasopasem does not receive regulatory approval, our business may be harmed. We currently have no products that are approved for commercial **, and we may not be** sale - **able to generate any revenue** . **•** We **do not have** expect that a substantial portion of our efforts **own manufacturing capabilities** and expenditures over the next few years will be devoted to the advancement of avasopasem, through the regulatory approval process, as well as the commercialization of avasopasem following regulatory approval, if received. We cannot be certain that avasopasem will receive regulatory approval, or be successfully commercialized even if we receive regulatory approval. We have not completed the development of any product candidates and we may never be able to develop marketable products. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of products are, and will remain, subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market avasopasem in the United States until we receive approval of a New Drug Application, or NDA, or in any foreign country until we receive the requisite approvals from the appropriate authorities in such countries for marketing authorization. We have not yet demonstrated our ability to obtain regulatory approval for any of our product candidates, and there can be no assurance that the results from our Phase 3 ROMAN trial together with the randomized Phase 2b GT- 201 trial of avasopasem will be sufficient for the FDA to approve the NDA for the reduction of SOM in patients with HNC that we submitted to the FDA in December 2022. While we are currently continuing our ongoing clinical trials, the COVID- 19 pandemic and related precautions have directly or indirectly impacted the timeline for certain of our clinical trials of avasopasem. We delayed the initiation of the Phase 2a multi- center trial in Europe assessing the safety of avasopasem in patients with HNC undergoing standard- of- care radiotherapy due to concerns with clinical trial enrollment in Europe during the COVID- 19 pandemic. The first patient was dosed in this trial in June 2020, and target enrollment was decreased to approximately 35 patients due to this delay. This trial was expected to contribute to the safety database for avasopasem in patients with HNC receiving radiotherapy. As a result of the delay in initiating the trial in Europe, the target enrollment for the ROMAN trial was increased to approximately 450 patients in order to ensure we were positioned to maintain the overall planned size of the safety database in a timely manner. While our Phase 3 ROMAN trial did demonstrate a statistically significant difference for the active 90 mg dose compared to placebo for the primary endpoint and a key secondary endpoint, we do not know whether the FDA will find these results together with the results from the randomized Phase 2b GT- 201 trial of avasopasem in patients with HNC sufficient to approve the NDA for avasopasem for the reduction of SOM in patients with HNC. In December 2022, we submitted to the FDA the NDA for avasopasem for the reduction of SOM in patients with HNC. Obtaining approval of an NDA or similar regulatory approval is an extensive, lengthy, expensive and inherently uncertain process, and the FDA or other foreign regulatory authorities may delay, limit or deny approval of any of our current or

future product candidates for many reasons, including: • we may not be able to demonstrate that avasopasem is effective as treatments for any of our targeted indications to the satisfaction of the FDA or other relevant regulatory authorities; • the relevant regulatory authorities may require additional pre- approval studies or clinical trials, which would increase our costs and prolong our development timelines; • the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or other relevant regulatory authorities for marketing approval; • the FDA or other relevant regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials; • the contract research organizations, or CROs, that we retain to conduct clinical trials may take actions outside of our control, or otherwise commit errors or breaches of protocols, that materially adversely impact our clinical trials and ability to obtain market approvals; • the FDA or other relevant regulatory authorities may not find the data from preclinical studies or clinical trials sufficient to demonstrate that the clinical and other benefits of avasopasem outweigh their safety risks; • the FDA or other relevant regulatory authorities may not be convinced that avasopasem has an acceptable safety profile; • the FDA or other relevant regulatory authorities may disagree with our interpretation of data or significance of results from the preclinical studies and clinical trials of avasopasem, or may require that we conduct additional studies; • the FDA or other relevant regulatory authorities may not accept data generated from our clinical trial sites; • if our NDA or other foreign application is reviewed by an advisory committee, the FDA or other relevant regulatory authority, as the case may be, may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA or other relevant regulatory authority, as the case may be, require, as a condition of approval, additional nonclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions; • the FDA or other relevant regulatory authorities may require additional post- marketing studies, which would be costly; • the FDA or other relevant regulatory authorities may identify deficiencies in the manufacturing processes or facilities of our third- party manufacturers; and • the FDA or other relevant regulatory authorities may change their approval policies or adopt new regulations. Clinical drug development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of earlier studies and trials may not be predictive of future trial results. If development of our product candidates is unsuccessful or delayed, we may be unable to obtain required regulatory approvals and be unable to commercialize our product candidates on a timely basis, if at all. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure or delay can occur at any time during the clinical trial process. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier preclinical studies or clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. The results of preclinical studies and clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we have agreements with our CROs governing their committed activities, and the ability to audit their performance, we have limited influence over their actual performance. We rely on third **parties** - party vendors, such as CROs, scientists and collaborators to provide us with significant data **produce additional clinical supplies, if needed,** and **commercial supplies of avasopasem and our** other **product candidates** information related to our preclinical studies or clinical trials and our business . If such **This reliance on** third parties provide inaccurate, misleading **increases the risk that we will not have sufficient quantities of** or **our product candidates** incomplete data, our - **or** business, prospects **such quantities at** and - **an** results of operations **acceptable cost, which** could **delay, prevent or impair our development or commercialization efforts. • The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate, or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability may** be materially adversely affected. **• The successful commercialization of avasopasem** For - **or** example, **any other product candidates will depend** in **part** October 2021, we announced topline data from the Phase 3 ROMAN trial of avasopasem in SOM and reported that the trial did not achieve statistical significance on the **extent to which governmental authorities** primary endpoint. Upon further analysis of the ROMAN data, an **and health insurers establish coverage** error by the CRO was identified in the statistical program. Correction of this error yielded the correct , statistically significant p- values for the primary and a key secondary endpoint. We announced the correct topline results in December 2021. We may experience delays in initiating our clinical trials and we cannot be certain that the trials or any other future clinical trials for our product candidates will begin on time, need to be redesigned, enroll an adequate number of patients on time **reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement** or **for our product candidates** be completed on schedule , if **approved, could limit** at all. Clinical trials can be delayed or **our ability to market those products and decrease** terminated for a variety of reasons, including delay or **our ability** failure related to : **generate revenue.** • **We face substantial competition** the FDA or comparable foreign regulatory authorities , such as the competent authorities of the member states of the EU, disagreeing as to the design or implementation of our clinical trials; • the size of the study population for further analysis of the study' s primary endpoints; • obtaining regulatory approval to commence a trial; • reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • obtaining institutional review board, or IRB, or ethics committee approval at each site; • recruiting suitable patients to participate in a trial; • having patients complete a trial or return for post- treatment follow- up; • clinical sites

deviating from trial protocol or dropping out of a trial; • addressing patient safety concerns that arise during the course of a trial; • addressing any conflicts with new or existing laws or regulations; • adding a sufficient number of clinical trial sites; or • manufacturing sufficient quantities of product candidate for use in clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities, such as the competent authorities of the member states of the EU. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, such as the competent authorities of the member states of the EU, resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Further, conducting clinical trials in foreign countries, as we plan to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. If we experience delays in the completion, or termination, of any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. The United Kingdom, or UK, is no longer part of the EU, and since the end of the Brexit transition period on January 1, 2021, the EU regulatory regime no longer applies in Great Britain (England, Wales and Scotland). Under the terms of the Ireland / Northern Ireland Protocol, the provisions of the CTR generally apply to clinical trials taking place in Northern Ireland. It is currently unclear to what extent the UK Government will seek to align the regulations in Great Britain with the EU CTR. The Great Britain regulatory framework in relation to clinical trials is still derived from the EU Clinical Trials Directive (as implemented into Great Britain law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency, or MHRA, carried out an eight- week consultation on a set of proposals aimed at improving and strengthening the clinical trials regime across the UK. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is closely watched and will determine whether the UK chooses to align with the EU CTR or diverge from it to maintain regulatory flexibility. A decision by the UK Government not to closely align its regulations with the new EU approach may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and / or make it harder to seek a MA in the EU for our product candidates on the basis of clinical trials conducted in the UK. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. If we encounter difficulties or delays enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including: • the patient eligibility criteria defined in the protocol; • the size of the patient population required for analysis of the trial's primary endpoints; • the proximity of patients to study sites; • the design of the trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating; • our ability to obtain and maintain patient consents; and • the risk that patients enrolled in clinical trials will drop out of the trials before completion. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same

therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise --- **others discovering** provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies and early- stage clinical trials are primarily designed to test safety , **developing** to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and early clinical trials does not ensure that later, large- scale efficacy trials will be successful, nor - **or commercializing drugs before** does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having **more** successfully advanced through initial clinical trials. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial sufficient to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving promising results in preclinical studies and earlier- stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects. We plan to conduct clinical trials for our product candidates outside the United States and the FDA may not accept data from such trials. We have conducted certain of our clinical trials outside the United States, and we plan to conduct additional clinical trials outside the United States. For example, we conducted a Phase 1 dose and schedule escalation study of rucosopasem in healthy volunteers in Australia. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data by the FDA is subject to certain conditions. For example, for clinical trials not otherwise subject to an IND, such clinical trials must be conducted in accordance with good clinical practices, or GCP, requirements and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the U. S. population and U. S. medical practice, the clinical trials were performed by clinical investigators of recognized competence, and the data are considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. In addition, such clinical trials would be subject to the applicable local laws of the foreign jurisdictions where the clinical trials are conducted. There can be no assurance the FDA will accept data from clinical trials conducted outside of the United States. There can also be no assurance that **than** the comparable foreign regulatory authority in any jurisdiction in which we **do** seek marketing approval for our product candidates will accept data from clinical trials conducted outside such jurisdiction . If the FDA or any such foreign regulatory authority does not accept any such data, it would likely result in the need for additional clinical trials, which would be costly and time- consuming and delay aspects of our development plan. In addition, the conduct of clinical trials outside the United States could have a significant impact on us. Risks inherent in conducting international clinical trials include: • foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials; • administrative burdens of conducting clinical trials under multiple foreign regulatory schemes; • foreign exchange fluctuations; • manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; and • diminished protection of intellectual property in some countries. Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue clinical trials, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any. **iiiPage PART I** Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities, such as the EMA or the competent authorities of the member states of the EU. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. To date, patients treated with our product candidates have experienced drug- related side effects including lymphopenia, nausea, fatigue, oropharyngeal pain, constipation, radiation skin injury and vomiting. If unacceptable side effects arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted, or the DSMB could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment- related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly. Our clinical trials include cancer patients who are very sick and whose health may

deteriorate, and we expect that additional clinical trials of our other product candidates will include similar patients with potentially deteriorating health. It is possible that some may die during our clinical trials for various reasons, including because the patient's underlying disease continues to advance despite treatment, or because the patient experiences medical problems that may not be related to our product candidate. For example, during the treatment phase of our Phase 2b trial of avasopasem, there was one non- treatment- related death in each of the placebo, 30 mg treatment and 90 mg treatment arms. Even if the deaths are not related to our product candidate, the deaths could affect perceptions regarding the safety of our product candidates. In addition, if any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including: • regulatory authorities may suspend, withdraw or limit their approval of the product, or seek an injunction against its manufacture or distribution; • we may be required to recall a product or change the way such product is administered to patients; • additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof; • regulatory authorities may require the addition of labeling statements, such as a " black box " warning or a contraindication, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product; • we may be required to implement a REMS or similar risk management measures, or create a Medication Guide outlining the risks of such side effects for distribution to patients, or implement other changes to how a product is distributed or administered; • we may be subject to fines, injunctions or the imposition of civil or criminal penalties; • we could be sued and held liable for harm caused to patients; • the product may become less competitive; and • our reputation may suffer. Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business. Interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose interim, topline, or preliminary data from our clinical trials, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a full analyses of all data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline, or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim, top- line, or preliminary data and final data could significantly harm our business prospects. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our business in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects or financial condition may be harmed. The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations. The development, research, testing, manufacturing, labeling, approval, selling, import, export, marketing, promotion and distribution of drug products are subject to extensive and evolving regulation by federal, state and local governmental authorities in the United States, principally the FDA, and by foreign authorities, such as the EU institutions or the competent authorities of the member states of the EU, which regulations differ from country to country. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States or foreign jurisdictions until we receive regulatory approval of an NDA from the FDA or similar approval from foreign regulatory authorities. Obtaining regulatory approval of an NDA or a similar foreign application can be a lengthy, expensive and uncertain process. Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well- controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. The number of preclinical studies and clinical trials that will be required for FDA or a foreign regulatory authority' s approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all indications. The FDA or foreign regulatory authorities may also require us to conduct

additional studies or trials for our product candidates either prior to or post- approval, such as additional drug- drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States or abroad. We may experience difficulty in identifying and enrolling patients in such a trial, if one were to be required, which could interrupt, delay or halt the process of obtaining regulatory approval of our product candidates. The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates or require us to conduct additional preclinical studies or clinical testing or abandon a program for many reasons, including: • the FDA or the applicable foreign regulatory agency' s disagreement with the design or implementation of our clinical trials; • negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval; • serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; • our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication; • the FDA' s or the applicable foreign regulatory agency' s disagreement with the interpretation of data from preclinical studies or clinical trials; • our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks; • the FDA' s or the applicable foreign regulatory agency' s requirement for additional preclinical studies or clinical trials; • the FDA' s or the applicable foreign regulatory agency' s disagreement regarding the formulation, labeling and / or the specifications of our product candidates; • the FDA' s or the applicable foreign regulatory agency' s failure to approve the manufacturing processes or facilities of third- party manufacturers with which we contract; or • the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval. Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. Even if we receive FDA approval of an NDA or foreign marketing application for avasopasem or our other product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and / or in the case of the FDA, the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or a narrower patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates proceed through preclinical studies to late- stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, notification to the FDA or foreign regulatory authorities or approval by the FDA or foreign regulatory authorities. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue. For example, in an effort to optimize scale- up efficiencies for avasopasem, we implemented certain changes to the manufacturing process related to the order of addition of ingredients. However, subsequent to this manufacturing change trace amounts of visible fine particles were observed in the drug product. Following notification to the FDA in April 2019 that we had voluntarily suspended dosing of avasopasem in all active clinical trials until we were able to resolve the issue, our INDs for avasopasem were temporarily placed on clinical hold. While we have now modified the manufacturing process and the FDA lifted the clinical holds in August 2019, and subsequently we added a filtration step to the preparation procedure for both avasopasem and placebo before administration to trial subjects to remove any particles that might form in the future, there can be no assurance that a similar or different manufacturing issue will not occur and one or more of our programs will not be placed on clinical hold in the future. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and management resources, we focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of avasopasem and rucosopasem. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications for avasopasem or rucosopasem that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. While we have received Breakthrough Therapy Designation for avasopasem, we may not receive such designation for our other product candidates, and such designation for avasopasem or any other product candidate may not lead to a faster development or regulatory review or approval process and will not increase the likelihood that our product candidates will receive marketing approval. We have received Breakthrough Therapy Designation from the FDA for avasopasem for the reduction of SOM induced by radiotherapy. We may also seek

Breakthrough Therapy Designation for any other product candidates that we may develop. A Breakthrough Therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs or biologies, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For product candidates that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as Breakthrough Therapies also receive the same benefits associated with Fast Track designation, including eligibility for rolling review of a submitted NDA, if the relevant criteria are met. Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe that a product candidate meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the designation, or otherwise decide that the time period required for FDA review or approval will not be reduced. Similarly, our products may not qualify for similar programs in other jurisdictions, such as the PRIME scheme in the EU. We have received Fast Track Designation for avasopasem, and we may seek such designation for some or all of our other product candidates. We may not receive such designation, and even for those product candidates for which we do, it may not lead to a faster development or regulatory review or approval process and will not increase the likelihood that product candidates will receive marketing approval. We have received Fast Track Designation from the FDA for avasopasem for the reduction of the severity and incidence of radiation and chemotherapy- induced OM, and we may seek Fast Track Designation for some or all of our other product candidates. If a drug is intended for the treatment of a serious or life- threatening condition or disease, and preclinical or clinical data demonstrate the potential to address an unmet medical need, the product may qualify for Fast Track Designation, for which sponsors must apply. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team - **Item** during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA has broad discretion whether or not to grant this designation. Thus, even if we believe a particular product candidate is eligible for this designation, the FDA may decide not to grant it. Moreover, even if we do receive Fast Track Designation, we or our collaborators may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain approval. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while 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 grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions, such as the European Commission, or the competent authorities of the EU member states, must also approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials, as studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and / or receive applicable marketing approvals, our target market size will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Since the end of the Brexit transition period on January 1 , 2021, however, Great Britain (England, Scotland and Wales) has operated under a separate regulatory regime to the EU. EU laws regarding medicinal products only apply in respect of the United Kingdom to Northern Ireland (as set out in the Protocol on Ireland / Northern Ireland). The EU laws that have been transposed into United Kingdom law through secondary legislation remain applicable in Great Britain. While the United Kingdom has indicated a general intention that new laws regarding the development, manufacture and commercialization of medicinal products in the United Kingdom will align closely with EU law, there are limited detailed proposals for future regulation of medicinal products. The trade and cooperation agreement includes specific provisions concerning medicinal products, which include the mutual recognition of Good Manufacturing Practice, or GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued (such mutual recognition can be rejected by either party in certain circumstances) but does not foresee wholesale mutual recognition of United Kingdom and EU pharmaceutical regulations. For example, it is not clear to what extent the United Kingdom will adopt legislation aligned with, or similar to, the EU CTR which became applicable on January 31, 2022 and which significantly reforms the assessment and supervision processes for clinical trials throughout the EU. Therefore, there remains political and economic uncertainty regarding to what extent the regulation of medicinal products will differ

between the United Kingdom and the EU in the future. Any divergences will increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. Brexit also materially impacted the regulatory regime with respect to the approval of our product candidates. Great Britain is no longer covered by the EU's procedures for the grant of marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). As of January 1, 2021, all existing centralized marketing authorizations were automatically converted into United Kingdom marketing authorizations effective in Great Britain and issued with a United Kingdom marketing authorization number on January 1, 2021 (unless marketing authorization holders opted out of this scheme). A separate marketing authorization is now required to market drugs in Great Britain. It is currently unclear whether the regulator in the United Kingdom, the MHRA is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Further, the United Kingdom's withdrawal from the EU has resulted in the relocation of the EMA from the United Kingdom to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the MHRA, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the EU and / or the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and / or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and / or EU for our product candidates, which could significantly and materially harm our business. Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval, or contain requirements for potentially costly post- market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Similar requirements may be requested by foreign regulatory authorities. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as continued compliance with current good manufacturing practice- grade, or cGMP, or similar foreign requirements and GCP requirements for any clinical trials that we conduct post- approval. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: • restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls; • fines, warning or untitled letters or holds on clinical trials; • refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals; • product seizure or detention, or refusal to permit the import or export of our product candidates; and • injunctions or the imposition of civil or criminal penalties. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability. Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business. The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's and foreign regulatory authorities' ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Separately, in response to the COVID- 19 pandemic, the FDA postponed most inspections of domestic and foreign

manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspection activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID- 19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. If we are found or alleged to have improperly promoted off- label uses, we may become subject to significant liability. The FDA and other regulatory agencies, including the competent authorities of the EU member states, strictly regulate the promotional claims that may be made about prescription products, as our product candidates would be, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product' s approved labeling. Physicians may nevertheless prescribe such drugs to their patients in a manner that is inconsistent with the approved label. For example, if we obtain approval for avasopasem for the reduction in the incidence of SOM in patients with locally advanced HNC receiving radiotherapy, we may pursue a strategy for avasopasem for the reduction of radiotherapy- induced esophagitis by presenting clinical data to entities like the National Comprehensive Cancer Network, or NCCN, to support use of avasopasem under these circumstances as a medically accepted indication in published drug compendia, notwithstanding the fact that we may not seek approval for avasopasem for radiotherapy- induced esophagitis by the FDA. Even if we are successful in obtaining Category 1 or Category 2A status from NCCN for avasopasem for the reduction of esophagitis, we will nevertheless be restricted from marketing and promoting the product for the reduction of esophagitis unless and until it is approved by the FDA for such indication. If we are found to have promoted off- label uses, or if the government takes the position that our presenting clinical data related to off- label uses of avasopasem to NCCN or other drug compendia publishers to establish compendia- listed indications constitutes off- label promotion, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition. The same applies in foreign jurisdictions, including the EU. Risks Related to Our Dependence on Third Parties We rely, and will continue to rely, on third parties to conduct our clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. We have relied, and expect to continue to rely, on CROs for the conduct of preclinical studies and clinical trials of avasopasem, rucosopasem and / or any other product candidates that we may progress to clinical development. We expect to continue to rely on third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. We have no control over the ability of our CROs to maintain adequate quality control, quality assurance and qualified personnel. For example, in October 2021, we announced topline data from the Phase 3 ROMAN trial of avasopasem in SOM and reported that the trial did not achieve statistical significance on the primary endpoint. Upon further analysis of the ROMAN data, an error by the CRO was identified in the statistical program. Correction of this error yielded the correct, statistically significant p- values for the primary and a key secondary endpoint. We announced the correct topline results in December 2021. If our CROs and other third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, their standard operating procedures and policies, or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and foreign regulatory authorities require us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fails to comply

with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP or similar foreign conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or foreign regulatory authorities. The FDA or foreign regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or foreign regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or foreign regulatory authorities and may ultimately lead to the denial of marketing approval of avasopasem, rucosopasem and any other product candidates. We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue. We contract with third parties for the manufacture and supply of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not have any manufacturing facilities or personnel. We do not have any long- term contractual arrangements with manufacturers and instead rely on third parties to manufacture our product candidates on a purchase- order or work- order basis. We currently have limited manufacturing arrangements, and we cannot be certain that we will be able to establish redundancy in manufacturers for our product candidates, which could lead to reliance on a limited number of manufacturers for one or more of our product candidates. This reliance increases the risk that we will not have sufficient quantities of our drug candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We also expect to rely on third- party manufacturers or third- party collaborators for the manufacture of commercial supply of avasopasem, if approved, and any other product candidates for which we obtain marketing approval. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture our product candidates must be approved by the FDA or other regulatory authorities for the manufacture of our product candidates pursuant to inspections that will be conducted after we submit our NDA or comparable marketing application to the FDA or other regulatory authority. We do not have control over a supplier' s or manufacturer' s compliance with laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. If our current or future suppliers are unable to supply us with sufficient raw materials for our preclinical studies and clinical trials, we may experience delays in our development efforts as we locate and qualify new raw material manufacturers. We may be unable to establish any agreements with future third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, qualifying and validating such manufacturers may take a significant period of time and reliance on third- party manufacturers entails additional risks, including: • reliance on the third party for regulatory compliance and quality assurance; • the possible breach of the manufacturing agreement by the third party; • the possible misappropriation of our proprietary information, including our trade secrets and know- how; • the possible increase in costs for the raw materials or drug substance in avasopasem or any of our other product candidates; and • the possible termination or nonrenewal of any agreement by any third party at a time that is costly or inconvenient for us. Third- party manufacturers may not be able to comply with cGMP regulations or other regulatory requirements outside the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Our product candidates and any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. There are no assurances we would be able to enter into similar commercial arrangements with other manufacturers that operate under cGMP regulations or other regulatory requirements outside the United States and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We may seek collaborations with third parties for the development or commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates. We may seek third- party collaborators for the development and commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any collaboration arrangements include large and mid- size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control

over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose the following risks to us: • collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may not perform their obligations as expected, including compliance with all applicable regulatory requirements; • collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates; • a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products; • disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time- consuming and expensive; • collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation; • collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and • collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. If we seek, but are not able to establish, collaborations, we may have to alter our development and commercialization plans. Our product development programs and the potential commercialization of our product candidates will require substantial additional capital. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue. Risks Related to Commercialization Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for commercial success. If any of our product candidates, including avasopasem, receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including: • the timing of market introduction; • the efficacy, safety and potential advantages compared to alternative treatments; • our ability to offer our products for sale at competitive prices; • the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments; • the perception by members of the healthcare community, including physicians or patients, that the process of administering our product candidates, including our intravenous infusion procedure, is not unduly cumbersome; • the clinical indications for which our product candidates are approved; • product labeling or product insert requirements of the FDA or other regulatory authorities; •

limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities; • the limited number of infusion sites where our product candidates can be administered; • our ability to successfully develop, or make arrangements with third- party manufacturers for, commercial manufacturing processes for any of our product candidates that receive regulatory approval; • our ability to hire and retain a sales force in the United States; • the strength of marketing and distribution support; • the recognition of uses for our products as medically accepted indications in recognized drug compendia; • the availability of third- party coverage and adequate reimbursement for avasopasem and any other potential product candidates; • the prevalence and severity of any side effects; and • any restrictions on the use of our products together with other medications. If we are unable to establish our own sales, marketing and distribution capabilities, or enter into agreements with third parties to sell and market avasopasem or any other product candidates, we may not be successful in commercializing our product candidates if and when they are approved, and we may not be able to generate any revenue. We do not currently have a sales, marketing or distribution infrastructure. We have never sold, marketed or distributed any therapeutic products. To achieve commercial success for any approved product candidate, we will need to establish a sales and marketing organization. Under the amended Royalty Agreement with Blackstone, we are required to establish a trained sales force sufficiently in advance of any anticipated commercial launch in a country where we seek to commercialize avasopasem or related product candidates. We expect to build a specialized sales and marketing organization of approximately 40 sales representatives to market our product candidates to the approximately 5, 000 radiation oncologists in the United States. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any drug launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to commercialize our product candidates on our own include: • our inability to recruit and retain adequate numbers of effective sales and marketing personnel; • the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products; • our inability to equip medical and sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding applicable diseases and our future products; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; • our inability to develop or obtain sufficient operational functions to support our commercial activities; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we are unable to establish our own sales, marketing and distribution capabilities and are forced to enter into arrangements with, and rely on, third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we had developed such capabilities ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate, or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability may be materially adversely affected. The precise incidence and prevalence for all the conditions we aim to address with our product candidates are unknown and cannot be precisely determined. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new trials may change the estimated incidence or prevalence of these diseases. The total addressable market across all of our product candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of our product candidates approved for sale for these indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. The successful commercialization of avasopasem or any other product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third- party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for our products or procedures using our products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third- party payor not to cover or separately reimburse for our products or procedures using our products, could reduce physician utilization of our products once approved. Assuming there is

coverage for our product candidates or procedures using our product candidates by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future. Third- party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third- party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third- party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third- party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third- party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. Some third- party payors may require pre- approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our product candidates. No uniform policy for coverage and reimbursement for products exists among third- party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to set their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. Moreover, increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set. In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following: • an annual, non- deductible fee payable by any entity that manufactures or imports certain branded prescription drugs (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs; • new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting " transfers of value " made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members; • a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; • expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 % of the federal poverty level, thereby potentially increasing a manufacturer' s Medicaid rebate liability; • a new Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and • establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA

brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court' s decision, President Biden issued an Executive Order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional action is taken by Congress. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100 % of a drug' s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U. S. Congressional inquiries, and Congress has proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing. We expect that additional U. S. healthcare reform measures will be adopted in the future, any of which could limit the amounts paid for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties. Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We are evaluating the opportunities for the development and commercialization of our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product

candidates in foreign markets, we would be subject to additional risks and uncertainties, including: • our customers' ability to obtain reimbursement for our product candidates in foreign markets; • our inability to directly control commercial activities because we are relying on third parties; • the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements; • different medical practices and customs in foreign countries affecting acceptance in the marketplace; • import or export licensing requirements; • longer accounts receivable collection times; • longer lead times for shipping; • language barriers for technical training and the need for language translations; • 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 adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. In some countries, particularly the countries in Europe, 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 reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially. Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop. We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates that we may develop; • injury to our reputation and significant negative media attention; • regulatory investigations that could require costly recalls or product modifications; • withdrawal of clinical trial participants; • significant costs to defend the related litigation; • substantial monetary awards to trial participants or patients; • loss of potential revenue; • the diversion of management' s attention away from managing our business; and • the inability to commercialize any product candidates that we may develop. Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur and is subject to deductibles and coverage limitations. We anticipate that we will need to increase our insurance coverage when and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If we are unable to obtain insurance at acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which may materially and adversely affect our business and financial position. These liabilities could prevent or interfere with our commercialization efforts. Risks Related to Competition, Retaining Key Employees and Managing Growth We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do. The development and commercialization of new drugs and biologics is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or biologics that are pursuing the development of therapies in the fields in which we are interested. Some of these competitive products and therapies are based on entirely different scientific approaches to our approach. 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. Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources, a more established presence in the market, and more expertise in research and development, manufacturing, preclinical studies and clinical trials, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining highly qualified scientific, sales, marketing and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. 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 drugs that we or our collaborators may develop. Because our product candidates are designed to reduce normal tissue toxicity from radiotherapy, or to increase the anti- cancer efficacy, our commercial opportunities could also be reduced or eliminated if radiotherapy methods are improved in a way that reduces normal tissue toxicity or increases anti- cancer efficacy, or if new therapies are developed which effectively treat cancer with less or without normal tissue toxicity. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related products, market acceptance by physicians and patients, the level of generic competition and the availability of reimbursement from government and other third- party payors. Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. We have a limited operating history and are highly dependent on the research and development, clinical, commercial and business development expertise of the principal

members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The failure to recruit, or the loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. If we are not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or growth. We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations. We expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day- to- day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, certain employees may need to perform activities that are beyond their regular scope of work, and we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company. We may not be successful in executing our growth strategy to identify, discover, develop, in- license or acquire additional product candidates or our growth strategy may not deliver the anticipated results. We plan to source new product candidates that are complementary to our existing product candidates through our internal discovery program, or in- licensing or acquiring them from other companies or academic institutions. If we are unable to identify, discover, develop, in- license or acquire and integrate product candidates in accordance with this strategy, our ability to pursue this part of our growth strategy would be limited. Research programs and business development efforts to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. In- licensing and acquisitions of technology often require significant payments, expenses and will consume additional resources. We will need to devote a substantial amount of time and personnel to research, develop and commercialize any acquired technology, in addition to our existing portfolio of programs. Our research programs, business development efforts or licensing attempts may fail to yield additional complementary or successful product candidates for clinical development and commercialization for a number of reasons, including, but not limited to, the following: • our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates with a high probability of success for development progression; • we may not be able or willing to assemble sufficient resources or expertise to in- license, acquire or discover additional product candidates; • for product candidates we seek to in- license or acquire, we may not be able to agree to acceptable terms with the licensor or owner of those product candidates; • our product candidates may not succeed in preclinical studies or clinical trials; • we may not succeed in formulation or process development; • our product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive regulatory approval; • competitors may develop alternatives that render our product candidates obsolete or less attractive; • product candidates that we develop may be covered by third parties' patents or other exclusive rights; • product candidates that we develop may not allow us to leverage our expertise and our development and commercial infrastructure as currently expected; • the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop; • a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a product candidate may not be accepted as safe and effective by patients, the medical community or third- party payors. If any of these events occurs, we may not be successful in executing our growth strategy or our growth strategy may not deliver the anticipated results. Risks Related to Intellectual Property If we are unable to adequately protect our proprietary technology and product candidates, if the scope of the patent protection obtained is not sufficiently broad, or if the terms of our patents are insufficient to protect our product candidates for an adequate amount of time, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our product candidates may be materially impaired. We rely primarily upon a combination of patents, trademarks, trade secret protection, and other intellectual property rights as well as

nondisclosure, confidentiality and other contractual agreements to protect the intellectual property related to our brands, product candidates, including avasopasem and rucosopasem, and other proprietary technologies. Our success depends on our ability to develop, manufacture, market and sell our product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings asserting patents and other intellectual property rights in the pharmaceutical and biotechnology industries. We cannot assure you that our product candidates, including avasopasem and rucosopasem, will not infringe existing or future third- party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing our product candidates, including avasopasem and rucosopasem. There may also be issued patents or pending patent applications that we are aware of, but that we think are irrelevant to our product candidates, including avasopasem and rucosopasem, which may ultimately be found to be infringed by the manufacture, sale, or use of our product candidates, including avasopasem and rucosopasem. Moreover, we may face claims from non- practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. In addition, many of our product candidates, including avasopasem and rucosopasem, have a complex structure that makes it difficult to conduct a thorough search and review of all potentially relevant third- party patents. Because we have not yet conducted a formal freedom to operate analysis for patents related to our product candidates, we may not be aware of issued patents that a third party might assert are infringed by one of our current or future product candidates, which could materially impair our ability to commercialize our product candidates. Even if we diligently search third- party patents for potential infringement by our products or product candidates, including avasopasem or rucosopasem, we may not successfully find patents that our products or product candidates, including avasopasem or rucosopasem, may infringe. If we are unable to secure and maintain freedom to operate, others could preclude us from commercializing our product candidates. The process of obtaining patent protection is expensive and time- consuming, and we may not be able to prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations or products and may choose not to pursue patent protection in certain jurisdictions, and under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope and, in any event, any patent protection we obtain may be limited. As a result, in some jurisdictions some of our products currently or in the future may not be, protected by patents. We generally apply for patents in those countries where we intend to make, have made, use, offer for sale, or sell products and where we assess the risk of infringement to justify the cost of seeking patent protection. However, we may not accurately predict all the countries where patent protection would ultimately be desirable. If we fail to timely file a patent application in any such country or major market, we may be precluded from doing so at a later date. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories in which we have patent protection that may not be sufficient to terminate infringing activities. In addition, the actual protection afforded by a patent varies on a product- by- product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory- related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Furthermore, we cannot guarantee that any patents will be issued from any pending or future owned or licensed patent applications, or that any current or future patents will provide us with any meaningful protection or competitive advantage. Even if issued, existing or future patents may be challenged, including with respect to ownership, narrowed, invalidated, held unenforceable or circumvented, any of which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the length of terms of patent protection we may have for our product candidates, including avasopasem and rucosopasem, and technologies. Moreover, should we be unable to obtain meaningful patent coverage for clinically relevant infusion rates for avasopasem and rucosopasem in jurisdictions with commercially significant markets, our ability to extend and reinforce patent protection for these product candidates in those jurisdictions may be adversely impacted, which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the length of terms of patent protection we may have for those product candidates. Other companies may also design around technologies we have patented, licensed or developed. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our products or practicing our own patented technology. The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal, scientific and factual questions for which important legal principles remain unresolved. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights may be uncertain. The standards that the United States Patent and Trademark Office, or the USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly. Changes in either the patent laws, implementing regulations or the interpretation of patent laws may diminish the value of our rights. The legal systems of certain countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than United States law does. In addition, many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to " work " the invention in that country, or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. Because patent applications in the United States, Europe and many

other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to conceive or reduce to practice the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or pending patent applications. We can give no assurance that all of the potentially relevant art relating to our patents and patent applications has been found; overlooked prior art could be used by a third party to challenge the validity, enforceability and scope of our patents or prevent a patent from issuing from a pending patent application. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the validity, enforceability and scope of our patents in the United States, Europe and in other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against our competitors. Third parties may challenge any existing patent or future patent we own or license through adversarial proceedings in the issuing offices or in court proceedings, including as a response to any assertion of our patents against them. In any of these proceedings, a court or agency with jurisdiction may find our patents invalid and / or unenforceable, or even if valid and enforceable, insufficient to provide protection against competing products and services sufficient to achieve our business objectives. We may be subject to a third- party pre- issuance submission of prior art to the USPTO, or reexamination by the USPTO if a third party asserts a substantial question of patentability against any claim of a U. S. patent we own or license. The adoption of the Leahy- Smith America Invents Act, or the Leahy- Smith Act, in September 2011 established additional opportunities for third parties to invalidate U. S. patent claims, including inter partes review and post- grant review proceedings. Outside of the United States, patents we own or license may become subject to patent opposition or similar proceedings, which may result in loss of scope of some claims or the entire patent. In addition, such proceedings are very complex and expensive, and may divert our management' s attention from our core business. If any of our patents are challenged, invalidated, circumvented by third parties or otherwise limited or expire prior to the commercialization of our products, and if we do not own or have exclusive rights to other enforceable patents protecting our products or other technologies, competitors and other third parties could market products and use processes that are substantially similar to, or superior to, ours and our business would suffer. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep a competitive advantage. For example: • others may be able to develop products that are similar to, or better than, ours in a way that is not covered by the claims of our patents; • we might not have been the first to conceive or reduce to practice the inventions covered by our patents or pending patent applications; • we might not have been the first to file patent applications for our inventions; • any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; or • we may not develop additional proprietary technologies that are patentable. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. We currently in- license certain intellectual property from third parties to be able to use such intellectual property in our products and product candidates and to aid in our research activities. In the future, we may in- license intellectual property from additional licensors. We may rely on certain of these licensors to file and prosecute patent applications and maintain, or assist us in the maintenance of, patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in- licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted diligently or in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate, or support our efforts to initiate, an infringement proceeding against a third- party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer. We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time- consuming and unsuccessful. Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights, trade secrets or other intellectual property, or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. In some cases, it may be difficult or impossible to detect third- party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult. We may not be able to prevent, alone or with our licensees or any future licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party or a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates, including avasopasem and rucosopasem. Such a loss of patent protection could harm our business. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from exploiting the claimed subject matter at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent' s claims narrowly or decide that we do not have the right to stop the other party from exploiting its technology on the grounds that our patents do not cover such technology. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making, using, importing and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position,

business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. In any infringement, misappropriation or other intellectual property litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. We may not be able to detect or prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees. Our commercial success depends significantly on our ability to operate without infringing upon the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for or obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates, including avasopasem and ruxosopasem, and services. Numerous third- party patents exist in the fields relating to our products and services, and it is difficult for industry participants, including us, to identify all third- party patent rights relevant to our product candidates, including avasopasem and ruxosopasem, services and technologies. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, because some patent applications are maintained as confidential for a certain period of time, we cannot be certain that third parties have not filed patent applications that cover our product candidates, including avasopasem and ruxosopasem, services and technologies. Therefore, it is uncertain whether the issuance of any third- party patent would require us to alter our development or commercial strategies for our product candidates, including avasopasem and ruxosopasem, or processes, or to obtain licenses or cease certain activities. Patents could be issued to third parties that we may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing products using our technology. If any third- party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtain a license under the applicable patents, or until such patents expire or they are determined to be held invalid or unenforceable. Our failure to obtain or maintain a license to any technology that we require to develop or commercialize our current and future product candidates, including avasopasem and ruxosopasem, may materially harm our business, financial condition and results of operations. Furthermore, we would be exposed to a threat of litigation. From time to time, we may be party to, or threatened with, litigation or other proceedings with third parties, including non- practicing entities, who allege that our product candidates, including avasopasem and ruxosopasem, components of our product candidates, including avasopasem and ruxosopasem, services, and / or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. The types of situations in which we may become a party to such litigation or proceedings include: • we or our collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our product candidates, including avasopasem and ruxosopasem, or processes do not infringe those third parties' patents; • we or our collaborators may participate at substantial cost in International Trade Commission proceedings to abate importation of third- party products that would compete unfairly with our products; • if our competitors file patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, derivation or opposition proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position; • if third parties initiate litigation claiming that our processes or product candidates, including avasopasem and ruxosopasem, infringe their patent or other intellectual property rights, we and our collaborators will need to defend against such proceedings; • if third parties initiate litigation or other proceedings, including inter partes reviews, oppositions or other similar agency proceedings, seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their products, services, or technologies do not infringe our patents or patents licensed to us, we will need to defend against such proceedings; • we may be subject to ownership disputes relating to intellectual property, including disputes arising from conflicting obligations of consultants or others who are involved in developing our product candidates, including avasopasem and ruxosopasem; and • if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or product candidates, including avasopasem and ruxosopasem, infringe or misappropriate its patent or other intellectual property rights and / or that we breached our obligations under the license agreement, and we and our collaborators would need to defend against such proceedings. These lawsuits and proceedings, regardless of merit, are time- consuming and expensive to initiate, maintain, defend or settle, and could divert the time and attention of managerial and technical personnel, which could materially adversely affect our business. Any such claim could also force us to do one or more of the following: • incur substantial monetary liability for infringement or other violations of intellectual property rights, which we may have to pay if a court decides that the product candidate, service, or technology at issue infringes or violates the third party' s rights, and if the court finds that the infringement was willful, we could be ordered to pay up to treble damages and the third party' s attorneys' fees; • pay

substantial damages to our customers or end users to discontinue use or replace infringing technology with non- infringing technology; • stop manufacturing, offering for sale, selling, using, importing, exporting or licensing the product or technology incorporating the allegedly infringing technology or stop incorporating the allegedly infringing technology into such product, service, or technology; • obtain from the owner of the infringed intellectual property right a license, which may require us to pay substantial upfront fees or royalties to sell or use the relevant technology and which may not be available on commercially reasonable terms, or at all; • redesign our product candidates, including avasopasem and rucosopasem, services, and technology so they do not infringe or violate the third party' s intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; • enter into cross- licenses with our competitors, which could weaken our overall intellectual property position; • lose the opportunity to license our technology to others or to collect royalty payments based upon successful protection and assertion of our intellectual property against others; • find alternative suppliers for non-infringing products and technologies, which could be costly and create significant delay; or • relinquish rights associated with one or more of our patent claims, if our claims are held invalid or otherwise unenforceable. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays, or prohibit us from manufacturing, marketing or otherwise commercializing our products, services and technology. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows. In addition, we may indemnify our customers and distributors against claims relating to the infringement of intellectual property rights of third parties related to our product candidates, including avasopasem and rucosopasem. Third parties may assert infringement claims against our customers or distributors. These claims may require us to initiate or defend protracted and costly litigation on behalf of our customers or distributors, regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of our customers, suppliers or distributors, or may be required to obtain licenses for the product candidates, including avasopasem and rucosopasem, or services they use. If we cannot obtain all necessary licenses on commercially reasonable terms, our customers may be forced to stop using our products or services. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a material adverse effect on the price of our common stock. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. The occurrence of any of these events may have a material adverse effect on our business, results of operation, financial condition or cash flows. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed. In addition to patent and trademark protection, we also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. Because we expect to rely on third parties to manufacture our product candidates, including avasopasem and rucosopasem, and we expect to continue to collaborate with third parties on the development of our product candidates, including avasopasem and rucosopasem, we must, at times, share trade secrets with them. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them prior to disclosing our proprietary information, such as our consultants and vendors, or our former or current employees. These agreements typically limit the rights of third parties to use or disclose our confidential information, including our trade secrets. We also enter into confidentiality and invention assignment agreements with our employees and consultants. Despite these efforts, however, any of these parties may breach the agreements and disclose our trade secrets and other unpatented or unregistered proprietary information, and once disclosed, we are likely to lose trade secret protection. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to enforce trade secret protection. A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, operating results and financial condition. Additionally, we cannot be certain that competitors will not gain access to our trade secrets and other proprietary confidential information or independently develop substantially equivalent information and techniques. Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our existing and future product candidates, including avasopasem and rucosopasem, and processes. As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries 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. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy- Smith Act was signed into law. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, and switched the United States patent system from a " first- to- invent " system to a " first-to- file " system. Under a " first- to- file " system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had conceived or reduced to practice the invention earlier. The USPTO recently developed new regulations and procedures to govern administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy-

Smith Act, in particular, the first- to- file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. The Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our patents and pending patent applications. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Furthermore, the U. S. Supreme Court and the U. S. Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how the patent laws of the United States are interpreted. Similarly, foreign courts have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by United States and foreign legislative bodies. Those changes may materially affect our patents or patent applications and our ability to obtain additional patent protection in the future. The United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh- Dole Act. The federal government retains a " nonexclusive, nontransferable, irrevocable, paid- up license " for its own benefit. The Bayh- Dole Act also provides federal agencies with " march- in rights. " March- in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a " nonexclusive, partially exclusive, or exclusive license " to a " responsible applicant or applicants. " If the patent owner refuses to do so, the government may grant the license itself. We partner with a number of universities, including the University of Iowa, Northwestern University, and the University of Texas Southwestern Medical Center, with respect to certain of our research, development and manufacturing. While it is our policy to avoid engaging our university partners in projects in which there is a risk that federal funds may be commingled, we cannot be sure that any co- developed intellectual property will be free from government rights pursuant to the Bayh- Dole Act. If, in the future, we co- own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh- Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected. If we do not obtain patent term extensions in the United States under the Hatch- Waxman Act and in foreign countries under similar legislation with respect to our product candidates, including avasopasem and rucosopasem, thereby potentially extending the term of marketing exclusivity for such product candidates, including avasopasem and rucosopasem, our business may be harmed. In the United States, a patent that covers an FDA- approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, including avasopasem and rucosopasem, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Act, which permits a patent term extension of up to a maximum of five years beyond the normal expiration of the patent if the patent is eligible for such an extension under the Hatch- Waxman Act as compensation for patent term lost during development and the FDA regulatory review process, which is limited to the approved indication (and potentially additional indications approved during the period of extension) covered by the patent. This extension is limited to only one patent that covers the approved product, the approved use of the product, or a method of manufacturing the product. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request and the patent term may still expire before or shortly after we receive FDA marketing approval. If we are unable to extend the expiration date of our existing patents or obtain new patents with longer expiry dates, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, 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. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, including avasopasem and rucosopasem, or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our own, which would have a material adverse effect on our business. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. During trademark registration proceedings, our trademark application (s) may be rejected. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties can oppose pending trademark applications and seek to cancel registered trademarks. Opposition or cancellation proceedings may be

filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidate (s), including avasopasem and rucosopasem, in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. We may not be able to protect our rights in these trademarks and trade names, which we need in order to build name recognition with potential partners or customers in our markets of interest. In addition, third parties have used trademarks similar and identical to our trademarks in foreign jurisdictions and have filed or may in the future file for registration of such trademarks. If they succeed in registering or developing common law rights in such trademarks, and if we are not successful in challenging such third- party rights, we may not be able to use these trademarks to market our products in those countries. In any case, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may not be able to adequately protect our intellectual property rights throughout the world. Certain of our key patent families have been filed in the United States, as well as in numerous jurisdictions outside the United States. However, our intellectual property rights in certain jurisdictions outside the United States may be less robust. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, the requirements for patentability may differ in certain countries, particularly developing countries, and we may be unable to obtain issued patents that contain claims that adequately cover or protect our current or future product candidates, including avasopasem and rucosopasem. 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 life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market current or future product candidates, including avasopasem and rucosopasem. Consequently, we may not be able to prevent third parties from practicing our technology in all countries outside the United States, or from selling or importing products made using our technology in and into those other jurisdictions where we do not have intellectual property rights. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our product candidates, including avasopasem and rucosopasem, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology. We may not identify relevant third- party patents or may incorrectly interpret the relevance, scope or expiration of a third- party patent which might adversely affect our ability to develop and market our product candidates, including avasopasem and rucosopasem. We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third- party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates, including avasopasem and rucosopasem, in any jurisdiction. For example, U. S. patent applications filed before November 29, 2000 and certain U. S. patent applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates, including avasopasem and rucosopasem could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates, including avasopasem and rucosopasem, or the use of our products. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates, including avasopasem and rucosopasem. We may incorrectly determine that our product candidates, including avasopasem and rucosopasem, are not covered by a third- party patent or may incorrectly predict whether a third party' s pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates, including avasopasem and rucosopasem, and services. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates, including avasopasem and rucosopasem, and services. If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail

in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates, including avasopasem and ruconopasem, that are held to be infringing. We might, if possible, also be forced to redesign products, product candidates, including avasopasem and ruconopasem, or services so that we no longer infringe the third- party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. Patent terms may be inadequate to protect our competitive position on our product candidates, including avasopasem and ruconopasem, for an adequate amount of time. Patents have a limited lifespan, and the protection patents afford is limited. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non- provisional filing date. Even if patents covering our product candidates, including avasopasem and ruconopasem, are obtained, once the patent life has expired for patents covering a product or product candidate, we may be open to competition from competitive products and services. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Intellectual property rights do not necessarily address all potential threats to our business. While we seek broad coverage under our existing patent applications, there is always a risk that an alteration to products or processes may provide sufficient basis for a competitor to avoid infringing our patent claims. In addition, patents, if granted, expire and we cannot provide any assurance that any potentially issued patents will adequately protect our product candidates, including avasopasem and ruconopasem. Once granted, patents may remain open to invalidity challenges including opposition, interference, re- examination, post- grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked or may lose the allowed or granted claims altogether. In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative: • others may be able to develop and / or practice technology that is similar to our technology or aspects of our technology, but that are not covered by the claims of the patents that we own or control, assuming such patents have issued or do issue; • we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed; • we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our pending patent applications will not lead to issued patents; • issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • third parties performing manufacturing or testing for us using our product candidates, including avasopasem and ruconopasem, or technologies could use the intellectual property of others without obtaining a proper license; • parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property; • we may not develop or in- license additional proprietary technologies that are patentable; • we may not be able to obtain and maintain necessary licenses on commercially reasonable terms, or at all; and • the patents of others may have an adverse effect on our business. Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects. We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties. We do and may employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our licensors, competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know- how of others in their work for us, and we are not currently subject to any claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or product candidates, including avasopasem and ruconopasem. Such a license may not be available on commercially reasonable terms or at all. 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 and could result in customers seeking other sources for the technology or in ceasing from doing business with us. Our intellectual property agreements with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology. Certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology or affect financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, while we typically require our employees, consultants and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. To the extent

that we fail to obtain such assignments, such assignments do not contain a self- executing assignment of intellectual property rights or such assignment agreements are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property and this may interfere with our ability to capture the commercial value of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. We may be subject to claims that former collaborators or other third parties have an ownership interest in our patents or other intellectual property. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time- consuming. If we are unsuccessful, we could lose valuable rights in intellectual property that we regard as our own. We may not be successful in obtaining necessary intellectual property rights to future products through acquisitions and in- licenses. Although we intend to develop products and technology through our own internal research, we may also seek to acquire or in- license technologies to grow our product offerings and technology portfolio. However, we may be unable to acquire or in- license intellectual property rights relating to, or necessary for, any such products or technology from third parties on commercially reasonable terms or at all. In that event, we may be unable to develop or commercialize such products or technology. We may also be unable to identify products or technology that we believe are an appropriate strategic fit for our Company and protect intellectual property relating to, or necessary for, such products and technology. The in- licensing and acquisition of third- party intellectual property rights for product candidates, including avasopasem and rucosopasem, is a competitive area, and a number of more established companies are also pursuing strategies to in- license or acquire third- party intellectual property rights for products that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. If we are unable to successfully obtain rights to additional technologies or products, our business, financial condition, results of operations and prospects for growth could suffer. In addition, we expect that competition for the in- licensing or acquisition of third- party intellectual property rights for products and technologies that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We may be unable to in- license or acquire the third- party intellectual property rights for products or technology on terms that would allow us to make an appropriate return on our investment. Other Risks Related to Our Business The COVID- 19 pandemic has adversely impacted and could continue to adversely impact, our business, including our clinical trials, results of operations and financial condition. The COVID- 19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce. While we are currently continuing our ongoing clinical trials, the COVID- 19 pandemic and related precautions have directly or indirectly impacted the timeline for certain of our clinical trials. In April 2020, we delayed the initiation of the Phase 2a multi- center trial in Europe assessing the safety of avasopasem manganese in patients with HNC undergoing standard- of- care radiotherapy. The first patient was dosed in the trial in June 2020, and target enrollment was decreased to approximately 35 patients due to the delay. This trial was expected to contribute to the safety database for avasopasem in patients with HNC receiving radiotherapy. As a result of the delay in initiating the trial in Europe, the target enrollment for the ROMAN trial was increased to approximately 450 patients in order to ensure we are positioned to maintain the planned size of the safety database in a timely manner. We have since completed the enrollment in the Phase 2a trial in Europe and the ROMAN trial. We are continuing to monitor the impact of the COVID- 19 pandemic on our operations and ongoing clinical development activity, generally. As a result of the COVID- 19 pandemic, we may experience further disruptions that could severely impact our business, preclinical studies and clinical trials, including: • delays in receiving approval from local regulatory authorities to initiate our planned clinical trials; • delays or difficulties in enrolling patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • risk that participants enrolled in our clinical trials will acquire COVID- 19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; • interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non- essential), which may impact the integrity of subject data and clinical study endpoints; • interruption or delays in the operations of the FDA or foreign regulatory authorities, which may impact approval timelines; • interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing or supply shortages, production slowdowns, global shipping delays or stoppages and disruptions in delivery systems; • limitations on employee resources, including at our third- party vendors, that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people. • refusal of the FDA or foreign regulatory authorities to accept data from clinical trials in affected geographies; • impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and • delays or difficulties with equity offerings due to disruptions and uncertainties in the securities market. The extent to which the COVID- 19 pandemic may further impact our business, including our preclinical studies and clinical trials, results of operations and financial condition, will depend on future developments which are highly uncertain and

cannot be predicted with confidence. Such factors include but are not limited to the duration of the pandemic, travel restrictions, quarantines, business closures or business disruptions, the effectiveness of vaccines and vaccine distribution efforts, the availability and effectiveness of COVID- 19 testing, the ultimate impact of COVID- 19 on financial markets and the global economy, and the effectiveness of other actions taken in the United States and other countries to contain and treat the disease. Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item **Item 1A** or service, for which payment may be made, in whole or in part, under U. S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit, among other things, including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U. S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • the U. S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U. S. federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children' s Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician providers (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified- nurse midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; • analogous U. S. state laws and regulations, including: state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third- party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and • similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and

uncertainty about economic stability. A severe or prolonged economic downturn, such as the global financial crisis, 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, or cause our customers to delay making payments for our services. Doing business internationally involves a number of risks, including but not limited to: • multiple, conflicting and changing laws and regulations such as privacy regulations, tax laws and export and import restrictions; • employment laws, regulatory requirements and other governmental approvals, permits and licenses; • failure by us to obtain and maintain regulatory approvals for the use of our products in various countries; • additional potentially relevant third- party patent rights; • complexities and difficulties in obtaining protection and enforcing our intellectual property; • difficulties in staffing and managing foreign operations; • complexities associated with managing multiple payor reimbursement regimes, government payors or patient self- pay systems; • limits in our ability to penetrate international markets; • financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations; • natural disasters, political and economic instability, including wars, such as the conflict between Russia and Ukraine, terrorism, political unrest, outbreak of disease, such as the novel coronavirus, and boycotts; • curtailment of trade, and other business restrictions; • certain expenses including, among others, expenses for travel, translation and insurance; and • regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U. S. Foreign Corrupt Practices Act, its books and records provisions or its anti- bribery provisions. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity. Despite the implementation of security measures, our information technology systems and those of our third- party CMOs, CROs, contractors and consultants are vulnerable to attack, interruption and damage from computer viruses and malware (e. g. ransomware), malicious code, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation- state and nation- state- supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID- 19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. While we do not believe that we have experienced any significant system failure or accident, from time to time, we have been the target of cybersecurity breach attempts and we expect them to continue as cybersecurity threats have been rapidly evolving in sophistication and becoming more prevalent. We do not believe that these cybersecurity breaches have had a material impact on our operations, but future breaches may have such impact. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure or theft of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Federal, state and international laws and regulations could expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U. S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or

collectively, HIPAA. HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. While we do not believe we are currently acting or regulated as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, which govern the privacy, processing and protection of health- related and other personal information. For example, the CCPA went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches has increased the likelihood of, and risks associated with data breach litigation. Further, the CPRA generally went into effect on January 1, 2023 and significantly amends the CCPA. The CPRA imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance and business process changes may be required. Similar laws have passed in Virginia, Connecticut, Utah and Colorado and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. Our operations abroad, including our clinical trial programs outside the United States may also be subject to increased scrutiny or attention from data protection authorities. Our activities outside the United States impose additional compliance requirements and generate additional risks of enforcement for noncompliance. In Europe, the GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the European Economic Area, or EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease / change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and / or civil claims (including class actions). Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July 2020, the Court of Justice of the EU, or CJEU, limited how organizations could lawfully transfer personal data from the EU / EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses, or SCCs. In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU- US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we conduct our business, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. Further, from January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR, or UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i. e., fines up to the greater of € 20 million (£ 17. 5 million) or 4 % of global turnover. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us, our third- party CMOs, CROs, contractors, or consultants to comply with applicable federal, state or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our products. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage. Violations of or liabilities under environmental, health and safety laws and regulations could subject us to fines, penalties or other costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures, the handling, use, storage, treatment and disposal of hazardous materials and wastes and the cleanup of contaminated sites. Our operations involve the use of potentially hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We could incur substantial costs as a result of violations of or liabilities under environmental

requirements in connection with our operations or property, including fines, penalties and other sanctions, investigation and cleanup costs and third- party claims. Although we generally contract with third parties for the disposal of hazardous materials and wastes from our operations, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of changes to applicable laws and regulations and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results. There has been increasing public focus by investors, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition. In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted. Insurance policies are expensive and protect us only from some business risks, which leaves us exposed to uninsured liabilities. Some of the insurance policies we currently maintain include general liability, employment practices liability, property, workers' compensation, umbrella, and directors' and officers' insurance. These policies may not adequately cover all categories of risk that our business may encounter. Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and 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 due to liability. If we obtain marketing approval for avasopasem, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations. We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our social media policy or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property or result in public exposure of personal information of our employees, clinical trial patients, customers and others. Furthermore, negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image and goodwill. Any of these events could have a material adverse effect on our business, prospects, operating results and financial condition and could adversely affect the price of our common stock. Our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could harm our business. Misconduct by our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA and other comparable regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing,

discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective 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 such laws or regulations. Additionally, we are subject to the risk that a person or government 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 and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U. S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations. We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage, public health emergency, such as the novel coronavirus, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations. In general, under Section 382 of the Code, a corporation that undergoes an " ownership change, " generally defined as a greater than 50 % change by value in its equity ownership over a three- year period, is subject to limitations on its ability to utilize its pre change net operating losses, or NOLs, to offset future taxable income. Our existing NOLs may be subject to limitations arising from ownership changes that we might have undergone in the past. Future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Section 382 of the Code, further limiting our ability to utilize a material portion of the NOLs even if we attain profitability. We are a multinational company that faces complex taxation regimes in various jurisdictions. Audits, investigations, and tax proceedings could have a material adverse effect on our business, results of operations, and financial condition. We are subject to income and non- income taxes in multiple jurisdictions. Income tax accounting often involves complex issues, and judgment is required in determining our worldwide provision for income taxes and other tax liabilities. In particular, the jurisdictions in which we operate have detailed transfer pricing rules, which require that all transactions with non- resident related parties be priced using arm' s length pricing principles within the meaning of such rules. We could be subject to tax audits involving transfer pricing issues. We believe that our tax positions are reasonable and our tax reserves are adequate to cover any potential liability. However, tax authorities in certain jurisdictions may disagree with our position, including the propriety of our related party arm' s length transfer pricing policies and the tax treatment of corresponding expenses and income. If any of these tax authorities were successful in challenging our positions, we may be liable for additional income tax and penalties and interest related thereto in excess of any reserves established therefor, which may have a significant impact on our results and operations and future cash flow. Risks Related to Our Common Stock Our common stock may be delisted from The Nasdaq Global Market if we cannot maintain compliance with Nasdaq' s continued listing requirements, which could harm our business, the trading price of our common stock, our ability to raise additional capital and the liquidity of the market for our common stock. Our common stock is currently listed on The Nasdaq Global Market. To maintain the listing of our common stock on The Nasdaq Global Market, we are required to meet certain listing requirements, including related to the price of our common stock. On June 8, 2022, we received written notice, or the Initial Notice, from The Nasdaq Stock Market LLC, or Nasdaq, indicating that we were no longer in compliance with the minimum Market Value of Listed Securities, or MVLS, of $ 50, 000, 000 required for continued listing on The Nasdaq Global Market, as set forth in Nasdaq Listing Rule 5450 (b) (2) (A), or the MVLS Requirement. The Initial Notice had no immediate effect on the listing of our common stock, which continued to trade on The Nasdaq Global Market under the symbol " GRTX. " In accordance with Nasdaq Listing Rule 5810 (c) (3) (C), we had a period of 180 calendar days, or until December 5, 2022, or the Compliance Date, to regain compliance with the MVLS Requirement. To regain compliance, our MVLS had to close at $ 50, 000, 000 or more for a minimum of 10 consecutive business days prior to the Compliance Date. On December 6, 2022, we received a letter from Nasdaq indicating that we did not regain compliance with the MVLS Requirement by the Compliance Date and that, unless we request a hearing before a Nasdaq hearings panel, or Panel, to appeal Nasdaq' s delisting determination by December 13, 2022, trading of our common stock would be suspended on December 15, 2022, and our common stock would be delisted from The Nasdaq Global Market. On December 13, 2022, we requested a hearing before a Panel. On January 24, 2023, prior to the scheduled hearing date, we received a letter from Nasdaq notifying us that we had regained compliance with the MVLS Requirement, as our MVLS had closed at over $ 50, 000, 000 for 10 consecutive business days, and that the hearing had been cancelled. There can be no assurance that we will be able to maintain compliance with Nasdaq Listing Rule 5450 (b) (2) (A) or any other listing requirements, or satisfy the requirements necessary to transfer the listing of our common stock to The Nasdaq Capital Market. Delisting from the Nasdaq Global Market or any Nasdaq market could make trading our common stock more difficult for investors, potentially leading to declines in our share price and liquidity. In addition, without a Nasdaq market listing, stockholders may have a difficult time getting a quote for

the sale or purchase of our common stock, the sale or purchase of our common stock would likely be made more difficult and the trading volume and liquidity of our common stock could decline. Delisting from Nasdaq could also result in negative publicity and could also make it more difficult for us to raise additional capital. The absence of such a listing may adversely affect the acceptance of our common stock as currency or the value accorded by other parties. If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on an over- the- counter quotation system, such as the OTCQB market, where an investor may find it more difficult to sell our common stock or obtain accurate quotations as to the market value of our common stock. We cannot assure you that our common stock, if delisted from Nasdaq, will be listed on another national securities exchange or quoted on an over- the counter quotation system. Our directors, officers and principal stockholders own a significant percentage of our stock and, if they choose to act together, are able to exercise influence over matters submitted to stockholders for approval. Our officers, directors and principal stockholders each holding more than 5 % of our common stock, collectively, control approximately 38 % of our outstanding common stock as of December 31, 2022. Accordingly, these stockholders, if they act together, will be able to exert a significant degree of influence over our management and affairs of our company and most matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could attempt to delay or prevent a change in control of us, even if such change in control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of us or our assets, and might affect the prevailing market price of our common stock due to investors' perceptions that conflicts of interest may exist or arise. As a result, this concentration of ownership may not be in the best interests of our other stockholders. We are an " emerging growth company, " and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors. We are an " emerging growth company, " as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenues of $ 1. 235 billion or more, (b) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering, or IPO (December 31, 2024), (c) the date on which we have issued more than $ 1 billion in nonconvertible debt during the previous three years, or (d) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock that is held by non- affiliates exceeds $ 700 million as of the last business day of our most recently completed second fiscal quarter. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include: • not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act of 2002, or Section 404; • an exemption from compliance with the requirement of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor' s report on the financial statements; • providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced " Management' s Discussion and Analysis of Financial Condition and Results of Operations " disclosure; • reduced disclosure obligations regarding executive compensation; and • exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may choose to take advantage of some, but not all, of the available exemptions. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. 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 shares price may be more volatile. We are a " smaller reporting company " and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors. We are considered a " smaller reporting company. " We are therefore entitled to rely on certain reduced disclosure requirements, such as an exemption from providing selected financial data and executive compensation information. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. 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 prices may be more volatile. We have incurred and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives. As a public company, we have incurred, and particularly after we are no longer an " emerging growth company, " expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes- Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time- consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance. Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially 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 as appropriate, validate through testing that controls

are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm, as applicable, will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could cause us to need to restate our previously issued financial statements and could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing: • a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors; • no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates; • the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer; • the ability of our board of directors to alter our bylaws without obtaining stockholder approval; • the required approval of the holders of at least two- thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer' s own slate of directors or otherwise attempting to obtain control of us. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers, other employees or our stockholders to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, our amended and restated certificate of incorporation or our amended and restated bylaws, or (4) any action asserting a claim governed by the internal affairs doctrine. Under our amended and restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Securities Act, the Exchange Act, or the rules and regulations thereunder. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation and bylaws described above. These exclusive forum provisions may have the effect of discouraging lawsuits against us and our directors, officers and other employees. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation or bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provisions contained in our amended and restated certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. Additionally, the proposal to pay future dividends to stockholders will

effectively be at the sole discretion of our board of directors after taking into account various factors our board of directors deems relevant, including our business prospects, capital requirements, financial performance and new product development. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. General



We may acquire businesses, or products or product candidates, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions. We have acquired and in- licensed, and may acquire or in- license, additional businesses or products, from other companies or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition or license, we will achieve the expected synergies to justify the transaction. New tax legislation may impact our results of operations and financial condition. On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act (the " Tax Act "), which significantly reformed the U. S. Internal Revenue Code of 1986, as amended, or the Code. Among a number of significant changes to the current U. S. federal income tax rules, the Tax Act reduced the marginal U. S. corporate income tax rate from 35 % to 21 %, limited the deduction for net interest expense, shifted the United States toward a more territorial tax system, and imposed new taxes to combat erosion of the U. S. federal income tax base. The financial statements contained herein reflect the effects of the Tax Act based on current guidance. However, there remain uncertainties and ambiguities in the application of certain provisions of the Tax Act, and, as a result, we made certain judgments and assumptions in the interpretation thereof. More recently, on August 16, 2022, the United States enacted the Inflation Reduction Act introducing, among other changes, a 15 % corporate minimum tax on certain United States corporations and a 1 % excise tax on certain stock redemptions by United States corporations. As we further analyze the impact of the Tax Act, the Inflation Reduction Act and any new tax legislation and collect relevant information to complete our computations of the related accounting impact, we may make adjustments to the provisional amounts that could materially affect our results of operations and financial condition. An active trading market for our common stock may not be sustained. An active public trading market for our common stock may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair value of your shares. An inactive market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration. The price of our common stock is likely to be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock. Our share price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at a price that you consider reasonable. The market price for our common stock may be influenced by many factors, including: • the results of clinical trials for our product candidates; • delays in the commencement, enrollment and the ultimate completion of clinical trials; • the results and potential impact of competitive products or technologies; • our ability to manufacture and successfully produce our product candidates; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • the level of expenses related to any of our product candidates or clinical development programs; • variations in our financial results or those of companies that are perceived to be similar to us; • financing or other corporate transactions, or inability to obtain additional funding; • failure to meet or exceed expectations of the investment community; • regulatory or legal developments in the United States and other countries; • the recruitment or departure of key personnel; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the results of our efforts to discover, develop, acquire or in- license additional product candidates; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry and market conditions; • changes in voting control of our executive officers and certain other members of our senior management or affiliates who hold our shares; and • the other factors described in this " Risk Factors " section. If securities or industry analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our shares price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrades our shares or issues other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our common stock could decrease, which in turn could cause the price of our common stock or its trading volume to decline. Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in dilution of the percentage ownership of our stockholders and could cause our common stock price to fall. We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing additional common stock or other equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.