Risk Factors Comparison 2024-02-29 to 2023-03-02 Form: 10-K

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

Except for the historical information contained herein or incorporated by reference, this Annual Report and the information incorporated by reference contains forward- looking statements that involve risks and uncertainties. These statements include projections about our research, development and commercialization efforts, our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results may differ materially from those discussed here. Factors that could cause or contribute to differences in our actual results include those discussed in the following section, as well as those discussed in Part II, Item 7 entitled " Management' s Discussion and Analysis of Financial Condition and Results of Operations " and elsewhere throughout this Annual Report and in any other documents incorporated by reference into this Annual Report. You should consider carefully the following risk factors, together with all of the other information included or incorporated in this Annual Report. Each of these risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock. There may be additional risks that we do not presently know of or that we currently believe are immaterial which could also impair our business and financial position. An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment. Risks Related to Our Financial Condition and Need For Additional Capital **We** ~~Except for the third quarter of 2022, we~~ have incurred significant losses **in each year** since our inception **other than 2022** . We anticipate that we will continue to incur significant losses for the foreseeable future. We are a biopharmaceutical company focused primarily on developing ONC201 for the treatment of H3 K27M- mutant **diffuse** glioma as we also evaluate programs to advance from our earlier stage pipeline. We have incurred significant net losses in each year since our inception ~~prior to~~ **other than** 2022, including a net loss of $ ~~173~~ **82** . **1** ~~2~~ ~~million and $ 43. 5~~ million for the twelve months ended December 31, ~~2021~~ **2023** ~~and 2020, respectively~~ . **As of** ~~Our profitability for the twelve months ended~~ December 31, ~~2022~~ **2023** ~~was due primarily to a non- recurring event, the closing of our Asset Sale with Emergent. As of December 31, 2022~~ , we had an accumulated deficit of approximately $ ~~713~~ **795** . ~~4~~ **5** million. To date, with the exception of the Asset Sale, we have financed our operations primarily through the sale of equity securities and, to a lesser extent, through government funding, licensing fees, the sales of TEMBEXA product and debt. We have devoted most of our financial resources to research and development, including our preclinical development activities and clinical trials. We ~~may~~ **expect to** continue to incur losses and negative cash flows for the foreseeable future. The size of any loss will depend, in part, on the rate of future expenditures and our ability to generate revenues. In particular, we expect to incur substantial expenses as we seek to: • continue development and manufacturing activities related to imipridones, including ONC201 for the treatment of H3 K27M- mutant **diffuse** glioma, and other potential indications; • obtain regulatory approvals for ONC201 and other imipridones; • scale- up manufacturing capabilities for ONC201 and other imipridones; • identify and in-license additional product candidates to expand our research and development pipeline; • maintain, expand and protect our intellectual property portfolio; and • continue our internal research and development efforts and seek to discover additional product candidates. To become and remain profitable, we must succeed in developing and eventually commercializing products with significant market potential. This will require us to be successful in a range of challenging activities, including acquiring or discovering product candidates, completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates, and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities. We obtained regulatory approval for and initially commercialized TEMBEXA, however, none of our other product candidates have been commercialized. We may not succeed in developing additional product candidates or commercializing any product candidate. If we do not successfully develop or commercialize any product candidate, or if revenues from any products that do receive regulatory approvals are insufficient, we will not achieve profitability and our business may fail. In addition to these risks in the United States, assuming regulatory approval in other geographies, our revenues are also dependent upon the size of markets outside of the United States, as well as our ability to obtain market approval and achieve commercial success outside of the United States. Although we achieved profitability in 2022 as a result of the closing of our Asset Sale with Emergent **Biodefense Operations Lansing LLC (Emergent)** , **we were not profitable in 2023, and** we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment. Our ability to generate future revenues from product sales is uncertain and depends upon our ability to successfully develop, obtain regulatory approval for, and commercialize product candidates, and even if we generate future revenues, they may not be sufficient to lead to profitability. Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for and commercialize product candidates. We may not generate revenues from product sales for the foreseeable future. Our ability to generate future revenues from product sales depends heavily on our success in: • obtaining favorable results for and advancing development of imipridones, including ONC201 for the treatment of

H3 K27M- mutant **diffuse** glioma, and other potential indications; • obtaining United States regulatory approval for ONC201 and other pipeline assets; • obtaining foreign regulatory approval (s) for ONC201 and other pipeline assets; • generating, licensing or otherwise acquiring a pipeline of product candidates which progress to clinical development, regulatory approval, and commercialization. Conducting preclinical testing and clinical trials is a time- consuming, expensive and uncertain process that takes years to activate, enroll, and complete, and we may never successfully enroll a sufficient number of patients or generate the necessary data required to obtain regulatory approval and achieve product sales. Our anticipated development costs would likely increase if we do not obtain favorable results or if development of any product candidate is delayed. In particular, we would likely incur higher costs than we currently anticipate if development of any product candidate is delayed because we are required by the FDA or foreign regulatory authorities to perform studies or trials in addition to those that we currently anticipate, or we decide to conduct additional studies or trials for strategic reasons. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict with certainty the timing or amount of any increase in our anticipated development costs that will result should any additional trials be necessary. Further, any product candidate if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that may not be commercially available for a number of years, if at all. For any approved product candidate, we anticipate incurring significant costs in connection with commercialization. As a result, we cannot assure you that we will be able to generate revenues from sales of any approved product candidate, or that we will achieve or maintain profitability even if we do generate sales. If we fail to obtain additional financing, we could be forced to delay, reduce or eliminate our product development programs, seek corporate partners for the development of our product development programs or relinquish or license on unfavorable terms, our rights to technologies or product candidates. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time- consuming, expensive and uncertain process that takes years to complete. We believe that our existing capital available to fund operations will enable us to fund our current operating expenses and capital requirements for at least the next twelve months. Changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate, and our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expected, or because the FDA or foreign regulatory authorities require us to perform studies or trials in addition to those that we currently anticipate. In January 2021, we acquired Oncoceutics, Inc. (Oncoceutics), a privately- held, clinical- stage biotechnology company developing imipridones, a novel potential class of compounds. Oncoceutics' lead product candidate, ONC201, is currently being evaluated in multiple clinical studies including in the ~~recently launched~~ Phase 3 ACTION ~~study~~ **Study** , a registrational study for H3 K27M- mutant **diffuse** glioma. We are also pursuing additional external opportunities to build our pipeline of product candidates, and we may need to raise additional funds if we identify additional product candidates, which we may obtain through one or more equity offerings, debt financings, government or other third- party funding, strategic alliances and licensing or collaboration arrangements. Securing additional financing may divert our management from our day- to- day activities, which may adversely affect our ability to develop and commercialize our most advanced clinical compounds, or any other product candidate. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to: • significantly delay, scale back or discontinue the development or commercialization of ONC201, or any other product candidate; • seek corporate partners for ONC201, or any other product candidate at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or • relinquish or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects and on our ability to develop our product candidates. If we draw down on our credit facility with Silicon Valley Bank, the terms of our loan and security agreement place restrictions on our operating and financial flexibility, and failure to comply with covenants or to satisfy certain conditions may result in acceleration of our repayment obligations and foreclosure on our pledged assets, which could significantly harm our liquidity, financial condition, operating results, business and prospects and cause the price of our securities to decline. Our Loan and Security Agreement (the Loan Agreement) with Silicon Valley Bank, **now a division of First- Citizens Bank & Trust Company,** effective January 31, 2022 **, as amended on November 21, 2023** , requires us to comply with certain financial covenants, including requiring that we maintain specified liquidity and cash levels at certain times. The Loan Agreement also requires us to comply with a number of other covenants (affirmative and negative), including restrictive covenants that limit our ability to, among other things, incur additional indebtedness; merge or consolidate with or into any other organization or otherwise suffer a change in control; acquire, own or make investments; repurchase or redeem any class of stock or other equity interest; declare or pay any cash dividend or make a cash distribution on any class of stock or other equity interest; and transfer a material portion of our assets, in each case subject to exceptions. Our obligations under the Loan Agreement are secured by a first priority perfected security interest in substantially all of our assets other than our intellectual property, subject to certain exceptions. In addition to other specified events of default, and subject to limited exceptions, Silicon Valley Bank could declare an event of default upon our non- compliance with certain covenants or the occurrence of certain events that it may determine, in its sole discretion, to have a material adverse effect, including: a material adverse change in, or a material adverse effect on our business, property, assets or operations, taken as a whole; a material impairment of our ability to perform any of our obligations under the Loan Agreement; a material adverse effect upon the collateral for the loan or its value; or a material impairment of the enforceability or priority of the liens upon the collateral for the loan or the legality, validity, binding effect or enforceability of the Loan Agreement or related agreements. If we default under the credit facility, Silicon Valley Bank may accelerate all of our repayment obligations, which may require us to seek additional or alternate financing and / or modify our operational plans. We cannot guarantee that we will be able to comply with all of the covenants contained in the

Loan Agreement in the future, or secure waivers if or when required. If we are unable to comply with or obtain a waiver of any noncompliance under the Loan Agreement, Silicon Valley Bank could declare an event of default or require us to further renegotiate the Loan Agreement on terms that may be significantly less favorable to us, or we may be required to seek additional or alternative financing. If we were to seek additional or alternative financing, any such financing may not be available to us on commercially reasonable terms or at all. If we are unable to access funds to meet those obligations or to renegotiate our agreement, Silicon Valley Bank could foreclose on our pledged assets and we would have to immediately cease operations. In addition, during the continuance of an event of default, the then- applicable interest rate on the then- outstanding principal balance is subject to increase. Upon an event of default, Silicon Valley Bank could also require us to repay the loan immediately, together with a prepayment penalty, and other fees. If we were to renegotiate the agreement under such circumstances, the terms may be significantly less favorable to us. If we were liquidated, Silicon Valley Bank' s right to repayment would be senior to the rights of our stockholders to receive any proceeds from the liquidation. Any declaration by Silicon Valley Bank of an event of default could significantly harm our liquidity, financial condition, operating results, business, and prospects and cause the price of our securities to decline ~~. In September 2022, Silicon Valley Bank and the Company agreed to suspend the availability of future advances under the Loan Agreement until such time the parties mutually agree to amend the Loan Agreement to, among other things, adjust the borrowing base and reset the covenants~~ . We may incur additional indebtedness in the future. The debt instruments governing such indebtedness may contain provisions that are as, or more, restrictive than the provisions governing our existing indebtedness. If we are unable to repay, refinance or restructure our indebtedness when payment is due, Silicon Valley Bank could proceed against the collateral or force us into bankruptcy or liquidation. We routinely evaluate external assets to build our pipeline of product candidates and there can be no assurance that we will be successful in identifying or completing a transaction for a candidate, that any such transaction will result in additional value for our stockholders or that the process will not have an adverse impact on our business. In ~~early 2019, we initiated a review of external assets that could be added to our pipeline of product candidates. In January 2021, we acquired Oncoceutics, a privately- held, clinical- stage biotechnology company developing imipridones, including ONC201. In connection with this transaction, we are responsible for, and bear the future costs of, development and commercialization of the acquired compounds. These costs will be substantial, and we may require additional capital in order to pursue the development and commercialization of these compounds as planned. Moreover, the anticipated benefits of these transactions may never be realized due to the various risks and uncertainties associated with drug development detailed elsewhere in the risk factors. For example, in July 2019, we entered into a License and Development Agreement with Cantex Pharmaceuticals, Inc. pursuant to which we acquired exclusive worldwide rights to develop and commercialize DSTAT for any and all uses. In May 2022, we decided to discontinue the development of Dociparstat sodium (DSTAT) and the License and Development Agreement was subsequently terminated. In~~ addition to our current assets, we may in- license or acquire additional assets, engage in a merger or acquisition transaction, issue additional shares of our common stock, or engage in other potential actions designed to maximize stockholder value. Our continuing review of these matters may not result in the identification or consummation of any transaction. The process of reviewing external opportunities may be time consuming and disruptive to our business operations and, if we are unable to effectively manage the process, our business, financial condition and results of operations could be adversely affected. We could incur substantial expenses associated with identifying, evaluating, negotiating, and consummating potential transactions. There can be no assurance that any potential additional transaction, if consummated, will provide greater value to our stockholders than that reflected in the current price of our common stock. In addition, once any potential additional transaction is consummated, we are likely to incur substantial costs associated with future development and testing of any new product candidate, which may require us to raise additional capital. Risks Related to Clinical Development and Regulatory Approval All of our product candidates are still under clinical development and may not obtain regulatory approval or be successfully commercialized. We have not marketed, distributed or sold any of our current product candidates. Our most advanced product candidate is ONC201, which we are developing for the treatment of H3 K27M- mutant **diffuse** glioma. In November 2022, we initiated a Phase 3 clinical study of ONC201 **(the Phase 3 ACTION Study)** , and it is possible that a single trial to support regulatory approval may not be sufficient ~~as the standard is two adequate and well- controlled Phase 3 trials~~ . There is no guarantee that our current or future clinical trials will be approved by regulators, and no guarantee that they will be completed or, if completed, will be successful, or if successful, will result in an approval for the sale of any of our product candidates. The success of any of our product candidates will depend on several factors, including the following: • generating positive safety and efficacy data from our clinical trials of ONC201; • receipt of marketing approvals from the FDA and corresponding regulatory authorities outside the United States; • establishing commercial manufacturing capabilities; • acceptance of the product, if approved for marketing; • effectively competing with other therapies; • a continued acceptable safety profile of the product following approval; and • obtaining, maintaining, enforcing and defending intellectual property rights and claims. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, including ONC201, which would materially harm our business. We may be unable to obtain, or may be delayed in obtaining, regulatory approval for our most advanced clinical candidate: ONC201. In January 2021, we acquired Oncoceutics, a privately- held, clinical- stage biotechnology company developing imipridones, a novel potential class of compounds. ~~Oncoceutic~~ **Oncoceutics** ' s lead product candidate, ONC201, is currently being evaluated in the Phase 3 ACTION ~~study~~ **Study** , and multiple investigator- sponsored clinical studies. We have reached general agreement with the FDA on the design of the Phase 3 **ACTION** ~~study~~ **Study** ~~or studies~~ to support a potential approval for marketing. We have not yet reached agreement with foreign regulators regarding the adequacy of the planned studies, for any of our ~~most advanced~~ clinical candidates, with respect to a potential approval for marketing. We may be required to conduct additional clinical, nonclinical or manufacturing validation studies and submit those data before consideration of our application occurs. Depending on the extent of these or any other required studies, approval of any NDA or application that we

submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA and / or foreign health authorities to approve our NDA or foreign application. Any delay in obtaining, or an inability to obtain, regulatory approvals could prevent us from generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for ONC201, which would have a material adverse effect on our business and could potentially cause us to cease operations. We depend on the successful completion of clinical trials for our product candidates, including ONC201. The positive clinical results obtained for our product candidates in prior clinical studies may not be repeated in future clinical studies. Before obtaining regulatory approval for the sale of our product candidates, including ONC201, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In the case of ONC201, early studies were open label studies of brain tumor patients, whereas the ongoing **Phase 3** ACTION ~~study~~ **Study** is a double blinded, placebo- controlled, investigational study. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products. We may experience a number of unforeseen events during, or as a result of, clinical trials for our product candidates, that could adversely affect the completion of our clinical trials, including: • regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs; • we might be required to change one of our clinical research organizations (CROs) during ongoing clinical programs; • the number of subjects required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, or subjects may drop out of these clinical trials at a higher rate than we anticipate; • our third- party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the subjects are being exposed to unacceptable health risks, or other factors outside our control; • regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory or quality requirements; • the cost of clinical trials of our product candidates may be greater than we anticipate; • we may encounter agency or judicial enforcement actions which impact our clinical trials; • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or • our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators to suspend or terminate the trials. We do not know whether any clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our most advanced product candidates, including ONC201. If later stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for any of our product candidates may be adversely impacted. Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. We may experience delays in clinical trials at any stage of development and testing of our product candidates. Our planned clinical trials may not begin on time, have an effective design, enroll a sufficient number of subjects, or be completed on schedule, if at all. Events which may result in a delay or unsuccessful completion of clinical trials, including our currently planned or future clinical trials include: • inability to raise funding necessary to initiate or continue a trial; • delays in obtaining, or failure to obtain, regulatory approval of Investigational New Drug applications or to commence a trial; • delays in reaching agreement with the FDA and foreign health authorities on final trial design; • imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities; • delays caused by disagreements with existing CROs and / or clinical trial sites; • delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites; • delays in obtaining, or failure to obtain, required IRB or ethics committee (EC) approvals covering each site; • delays in recruiting suitable patients to participate in a trial; • delays in having subjects complete participation in a trial or return for post- treatment follow- up; • delays caused by subjects dropping out of a trial due to side effects or otherwise; • clinical sites declining to participate or dropping out of a trial to the detriment of enrollment; • agency or judicial enforcement actions against us; • changes in standard of care in specific diseases; • time required to add new clinical sites; and • delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials. If initiation or completion of any of our clinical trials for our product candidates, are delayed for any of the above reasons, our development costs may increase, our approval process could be delayed, any periods during which we may have the exclusive right to commercialize our product candidates may be reduced and our competitors may have more time to bring products to market before we do. Any of these events could impair our ability to generate revenues from product sales and impair our ability to generate regulatory and commercialization milestones and royalties, all of which could have a material adverse effect on our business. Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance. Adverse events (AEs) caused by our product candidates could cause us, other reviewing entities, clinical study sites or regulatory authorities to interrupt, delay or halt clinical studies and could result in the denial of regulatory approval. For example, in our Phase 2 study of ONC201, one serious adverse event, considered to be possibly ONC201- related by the investigator and unlikely to be ONC201- related by the sponsor, was identified. Full safety data collection and analysis for this cohort is ongoing. If an unacceptable frequency and / or severity of AEs are reported in our clinical trials for our product candidates, our ability to

obtain regulatory approval for product candidates may be negatively impacted. If any of our approved products cause serious or unexpected side effects prior to or after receiving market approval, a number of potentially significant negative consequences could result, including: • regulatory authorities may approve the product only with a risk evaluation and mitigation strategy (REMS), potentially with restrictions on distribution and other elements to assure safe use (ETASU); • regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in a form of a modified REMS; • regulatory authorities may require the addition of labeling statements, such as warnings or contraindications; • we may be required to change the way the product is administered or to conduct additional clinical studies; • we could be sued and held liable for harm caused to patients; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates. After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize any of our product candidates and we cannot, therefore, predict the timing of any future revenue from any of our product candidates, including ONC201. We cannot commercialize our product candidates, including ONC201, until the appropriate regulatory authorities have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for any of our product candidates. Delays may occur because we may not be able to obtain accelerated approval for our product candidates and large confirmatory studies may be needed to support accelerated approval or be conducted to pursue a first full approval. For ONC201, a companion diagnostic test may be needed to identify patients with H3 K27M- mutant **diffuse** glioma ~~before approval~~. Additional delays in the United States may result if any of our product candidates is brought before an FDA advisory committee, which could recommend restrictions on approval or recommend non- approval of the product candidate. In the EU context, an Oral Explanation during MAA review could extend approval timelines and result in a Negative Opinion. A re-examination procedure is available in the EU whereby a Negative Opinion could be over- turned and become a Positive Opinion. New rapporteurs would be selected for the product. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. As a result, we cannot predict when, if at all, we will receive any future revenue from commercialization of any of our product candidates. Failure by us or third- party collaborators to successfully develop, validate and obtain regulatory approval for companion diagnostics for use by oncologists could harm our ability to develop and commercialize ONC201. For ONC201, ~~a~~ standard of care diagnostic ~~test~~ **tests** ~~is~~ **are** used to identify patients with H3 K27M- mutant **diffuse** glioma. Currently, ~~that~~ **such** ~~test~~ **tests are** ~~is only~~ available as a Laboratory Developed Test, or LDT, that has not been cleared or approved by FDA **as a companion diagnostic test**. FDA may require approval of a companion diagnostic in connection with an approval of **an** ONC201 NDA. We intend to rely on third ~~-~~-parties for development of companion diagnostics for commercialization of ONC201, if required. Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices. Any failure by a third ~~-~~-party to obtain FDA clearance or approval for an H3 K27M mutation diagnostic test may impair our ability to meet FDA requirements for ONC201 and subsequently jeopardize or delay a potential marketing authorization. The FDA may determine that ONC201 or any of our other product candidates, even if approved for the designated rare pediatric disease prior to September 30, 2026, do not meet the eligibility criteria for a priority review voucher. Upon regulatory approval of a product candidate for a designated rare pediatric disease, neglected tropical disease, or medical countermeasure, the FDA may award to the sponsor of the treatment a transferable voucher that enables the bearer to priority review of another product candidate. The FDA has granted rare pediatric disease designation to ONC201 for treatment of H3 K27M- mutant **diffuse** glioma. Designation of a drug for a rare pediatric disease does not guarantee that an NDA for such drug will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the Federal Food, Drug, and Cosmetic Act (FDCA), we will need to request a rare pediatric disease priority review voucher in our original NDA for ONC201. The FDA may determine that an NDA for ONC201, if approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons: • treatment of H3 K27M- mutant **diffuse** glioma no longer meets the definition of a rare pediatric disease; • the NDA contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in an NDA; • the NDA is not deemed eligible for priority review; • the NDA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population (that is, if the NDA does not contain sufficient clinical data to allow for adequate labeling for use by the full range of affected pediatric patients); or • the NDA is approved for a different adult indication than the rare pediatric disease for which ONC201 is designated. The authority for the FDA to award rare pediatric disease priority review vouchers for drugs that have received rare pediatric disease designation prior to September 30, 2024 currently expires on September 30, 2026. Absent any legislative extension, if the NDA for ONC201 is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease priority review voucher, it will not be eligible for a priority review voucher **. In the event that the Company receives a priority review voucher for ONC201, any proceeds related to the voucher would be subject to potential adjustment according to the terms of our merger agreement with Oncoceutics**. Following regulatory approval for any of our product candidates, including ONC201, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties. Even if we obtain regulatory approval, the granting authority may still impose significant restrictions on the indicated uses, distribution or marketing of our product candidates, including ONC201, or impose ongoing requirements for potentially costly post- approval studies or post- market surveillance. For example, the labeling ultimately approved for our product candidates, will likely include restrictions on use due to the specific patient population and manner of use in which the drug was evaluated and the safety and efficacy data obtained in those evaluations. In addition, the distribution of any of our product candidates may be tightly controlled through a REMS with ETASU, which are required medical interventions or other actions healthcare professionals need to execute prior to prescribing or dispensing the drug to the

patient. Our product candidates will also be subject to additional ongoing regulatory requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record- keeping and reporting of safety and other post- market information. In the United States, the holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. If a REMS is required, the NDA holder may be required to monitor and evaluate those in the healthcare system who are responsible for implementing ETASU measures. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Moreover, EU and member countries impose strict restrictions on the promotion and marketing of drug products. The off- label promotion of medicinal products is prohibited in the U. S., EU and in other territories. Physicians, on the other hand, may prescribe products for off- label uses in the U. S. Although the FDA and other regulatory agencies do not regulate a physician' s choice of drug treatment made in the physician' s independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off- label uses of products for which marketing clearance has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with a product' s FDA approved labeling. The promotion of medicinal products that are not subject to a marketing authorization is also prohibited in the EU. Violations of the rules governing the promotion of medicinal products in the EU and in other territories could be penalized by administrative measures, fines and imprisonment. In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by regulatory authorities for compliance with Current Good Manufacturing Practices (cGMP), and adherence to commitments made in the application. If we, or a regulatory agency, discover previously unknown problems with a product, such as quality issues or AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following approval of any product candidates, a regulatory agency may: • issue an untitled or warning letter asserting that we are in violation of the law; • seek an injunction or impose civil or criminal penalties or monetary fines; • suspend or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve a pending application or supplements to an application submitted by us; • recall and / or seize product; or • refuse to allow us to enter into supply contracts, including government contracts. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and inhibit our ability to generate revenues. We may never obtain approval for or commercialize any of our products outside of the United States, nor does approval of any of our products outside the United States mean we will ever obtain approval for or commercialize any of our products inside the United States, all of which could limit our ability to realize their full market potential. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements on a country- by- country basis regarding safety and efficacy. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and **Chimerix has limited** ~~we do not have~~ experience in obtaining regulatory approval in any markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized. Conversely, approval by regulatory authorities outside the United States, such as the European Commission, does not ensure approval by the FDA. Moreover, clinical trials conducted outside the United States may not be accepted by the FDA. Coverage and adequate reimbursement may not be available for ONC201, or any of our other current or future product candidates, which could make it difficult for us to sell profitably, if approved. Market acceptance and sales of ONC201, or any other product candidates that we commercialize, if approved, will depend in part on the extent to which coverage and adequate reimbursement will be available from third- party payers, including government health administration authorities, managed care organizations and private health insurers. Third- party payers decide which therapies they will pay for and establish reimbursement levels. Third- party payers in the United States often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payer- by- payer basis. One payer' s determination to provide coverage for a drug does not assure that other payers will also provide coverage and adequate reimbursement for the drug. Additionally, a third- party payer' s decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Third- party payers are increasingly challenging the price, examining the medical necessity and reviewing the cost- effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Even if favorable coverage and reimbursement status is attained for our products candidates for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future **. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to**

companion diagnostics . We cannot be sure that coverage and reimbursement in the United States or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. Our relationships with investigators, health care professionals, consultants, third- party payers, and customers may be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers and others play a primary role in the recommendation and prescribing of any products for which we obtain marketing approval. Our current business operations and future arrangements with investigators, healthcare professionals, consultants, third- party payers 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 research, market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following: • the federal healthcare anti- kickback statute which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid; • the federal civil and criminal false claims laws, including the Federal Civil False Claims Act (False Claims Act) which permit private individuals to bring a civil action on behalf of the federal government to enforce certain of these laws thought civil whistleblower or qui tam actions and the Federal Civil Monetary Penalties Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government; • the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e. g., public or private) and knowingly or willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and their implementing regulations impose certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, and their business associates as well as their covered subcontractors; • the General Data Protection Regulation (GDPR), which impose obligations on companies in relation to the handling of personal data of individuals within the EU, along with related national legislation; • mandated healthcare professional payments reporting laws and / or requirements throughout global jurisdictions, including EU member states, in which we conduct research and development and / or other business activities; • the FDCA which prohibits, among other things, the adulteration or misbranding of drugs and devices; • the federal transparency law, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies to report to the Centers for Medicare & Medicaid Services (CMS) information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and • analogous 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 state governmental and non- governmental third- party payers, 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 federal government; state and local laws that require the registration of pharmaceutical sales representatives; state laws and regulations that require 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 laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA. Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations 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 these or any other health regulatory laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and / or divert our management' s attention from the operation of our business. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they also may be subject to significant criminal, civil or administrative sanctions, including, but not limited to, exclusions

from government funded healthcare programs, which could also materially affect our business. Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any products for which we obtain marketing approval. For example, in March 2010, the ACA was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. However, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021, the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. It is possible that the ACA will be subject to additional challenges in the future. It is unclear how any such challenges and other litigation, and the healthcare reform measures of the Biden administration will impact the ACA and our business. Legislative and regulatory proposals have also been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U. S. Congressional inquiries, presidential executive orders, and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order with multiple provisions aimed at prescription drugs. In response to this executive order, in September 2021, the U. S. Department of Health and Human Services (DHHS) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions DHHS can take to advance these principles. In addition, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law, which among other things, (1) directs the DHHS to negotiate the price of certain single- source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. **The IRA permits DHHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. DHHS has and will continue to issue and update guidance as these programs as implemented.** These provisions ~~will take~~ **have begun taking** effect progressively starting in fiscal year 2023 **. On August 29, 2023, DHHS announced the list of the first ten drugs that will be subject to price negotiations** , although ~~they~~ - **the** ~~may be~~ **Medicare drug price negotiation program is currently** subject to legal challenges. It is ~~currently~~ unclear how **certain aspects of** the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. While the **IRA** ~~Inflation Reduction Act of 2022~~ predominantly focuses on controlling spending of drugs that are covered by Medicare, and our product candidates, if approved, are not expected to target the Medicare population, other similar legislation may be implemented in the future that may be broader in scope and may adversely affect our operations, including our ability to commercialize our product candidates, if approved, successfully. ~~Additionally,~~ **In response to** the Biden administration ~~released an additional~~ **' s October 2022** executive order **,** on ~~October~~ **February** 14, ~~2022~~ **2023** , ~~directing~~ DHHS **released** ~~to submit~~ a report **outlining** ~~on how the three Center for Medicare and Medicaid Innovation can be further leveraged to test~~ new models for **testing by the CMS Innovation Center which will be evaluated on their ability to** ~~lowering~~ --- **lower** ~~drug~~ **the** ~~costs~~ - **cost** ~~for both Medicare~~ **of drugs, promote accessibility,** and ~~Medicaid beneficiaries~~ **improve quality of care** . It is unclear whether **the models** ~~this executive order or similar policy initiatives~~ will be ~~implemented~~ **utilized in any health reform measures** in the future **. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework** . At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological 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 **. For example, on January 5, 2024, the FDA approved Florida' s Section 804 Importation Program (SIP) proposal to import certain pharmaceutical products from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs** . Such reform efforts are likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria, lower reimbursement, and additional downward pressure on the price that we receive for any future approved product. We cannot predict what healthcare reform initiatives may be adopted in the future. Risks Related to Our Reliance on Third Parties We rely on third- party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates. We do not own or operate, and we do not expect to own or operate, facilities for product manufacturing, storage and distribution, or testing with respect to our product candidates, including ONC201. In the past, we have relied on third- party manufacturers for supply

of our preclinical and clinical drug supplies. We expect that in the future we will continue to rely on such manufacturers for drug supply that will be used in clinical trials and for commercialization of any of our product candidates that receive regulatory approval. Our reliance on third- party manufacturers entails risks, including: • inability to meet our product specifications and quality requirements consistently; • delay or inability to procure or expand sufficient manufacturing capacity; • manufacturing and product quality issues related to scale- up of manufacturing; • costs and validation of new equipment and facilities required for scale- up; • failure to comply with cGMP and similar foreign standards; • inability to negotiate manufacturing agreements with third parties under commercially reasonable terms; • termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; • reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms; • lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier; • operations of our third- party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier, or other factors outside our control; • carrier disruptions or increased costs that are beyond our control; and • failure to deliver our products under specified storage conditions and in a timely manner. Any of these events could lead to clinical study delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA or equivalent foreign regulator action, including injunction, recall, seizure, or total or partial suspension of production. Manufacturing issues may arise that could increase product and regulatory approval costs or delay or impair commercialization of ONC201 or our other product candidates. We plan to validate ONC201 drug substance and drug product processes prior to approval at our selected vendors. It is our expectation that only one supplier of drug substance and one supplier of drug product will be qualified as vendors for ONC201 with the FDA. If supply is interrupted, there could be a significant disruption in the clinical supply. An alternate vendor would need to be qualified which could result in a further delay. As more batch data is generated during both pre- and post- validation for both the drug substance and drug products, and as additional stability data is collected, issues may arise in our processes and stability programs which could require resolution in order to proceed with our planned clinical trials and obtain regulatory approval for the commercial marketing of our products and product candidates. In the future, we may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical program and regulatory approval for our products and product candidates, increases in our operating expenses, or failure to obtain or maintain approval for ONC201. The anticipated benefits of the sale of our TEMBEXA program and related assets may not be realized fully or at all or may take longer to realize than expected. In September 2022, we completed the sale of our TEMBEXA program and related assets to Emergent ~~Biodefense Operations Lansing LLC (Emergent)~~. Under the terms of the sale, we are entitled to contingent consideration, including milestone payments and royalties, dependent upon the further development and commercial success of TEMBEXA. Accordingly, our ability to receive the contingent consideration will depend, in part, on Emergent' s ability to successfully develop and commercialize TEMBEXA. If Emergent is unable to successfully or timely integrate TEMBEXA operations into its business, it may not be able to realize the revenue growth, milestone achievements, synergies and other anticipated benefits resulting from the Asset Sale, and consequently, we may not receive all, or any, of the contingent payments under the **Asset** Purchase Agreement. The milestones set forth in the **Asset** Purchase Agreement may not be achieved on a timely basis, if at all, and we may not receive any future contingent payments. Any failure to achieve such milestones, or a perception that the milestones may not be achieved, may adversely affect our business and the value of our common stock. Moreover, in 2019, we entered into a licensing arrangement with SymBio Pharmaceuticals (SymBio), whereby SymBio is responsible for the future development and commercialization of TEMBEXA for human diseases other than orthopoxviruses, including smallpox. In connection with the sale of TEMBEXA worldwide rights to Emergent, our rights and obligations under the SymBio license agreement were assumed by Emergent. We could receive up to $ 12. 5 million from Emergent in brincidofovir regulatory milestones related to the SymBio license agreement. Our right to receive milestone payments under the Asset Purchase Agreement depends on the achievement of certain regulatory milestones by SymBio in the licensed indications. The development and commercialization of the non- orthopox uses of TEMBEXA in humans and our ability to receive potential milestone payments under the Asset Purchase Agreement, would be adversely affected if SymBio: • lacks or does not devote sufficient time and resource to the development of TEMBEXA; • lacks or does not devote sufficient capital to fund the development of TEMBEXA; • develops, either alone or with others, products that compete with TEMBEXA; • fails to gain the requisite regulatory approvals for TEMBEXA; • does not conduct its activities in a timely manner; • terminates its license with Emergent; • does not effectively pursue and enforce intellectual property rights relating to TEMBEXA; or • merges with a third- party that wants to terminate the collaboration. We have limited or no control over the occurrence of any of the foregoing. If any of these issues arise, it may delay or eliminate our ability to receive the regulatory milestones in the Asset Purchase Agreement. Emergent may not adequately perform according to the terms of the BARDA ~~Contract~~ **Agreement**, and we might be required to guarantee performance of all obligations that Emergent assumed under novation. As required by U. S. government contracting regulations, the novation agreement for the BARDA ~~Contract~~ **Agreement** includes a clause requiring that Chimerix, as transferor, guarantee Emergent' s performance of the BARDA ~~Contract~~ **Agreement**. If Emergent were to fail to manufacture or deliver treatment courses of TEMBEXA, fail to properly respond to a product recall, or breach other performance obligations, BARDA may require that we perform instead, which may cause us to file claims under our insurance policies, divert the attention of our management from company priorities, expend additional resources engaging vendors, require additional legal agreements with Emergent to enable Chimerix to resume title to TEMBEXA and control of supply chain vendors necessary for performance, incur additional legal fees, among other unplanned expenses which could delay or prevent our completion of our priority clinical programs, as well as result in reputational harm. We rely on third parties to conduct, supervise and monitor our clinical studies and related data, and if those third parties perform

in an unsatisfactory manner, it may harm our business. We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our ongoing clinical programs for our product candidates, as well as the execution of nonclinical studies. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with the FDA' s guidance for clinical trials conducted within the jurisdiction of the United States (or the foreign regulatory authority equivalent for clinical trials conducted outside the jurisdiction of the United States), which follows the International Council for Harmonization Good Clinical Practice (ICH GCP), which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces the ICH GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with the ICH GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any 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 ONC201 or any other product candidates. Disagreements with our CROs over contractual issues, including performance, compliance or compensation could lead to termination of CRO agreements and / or delays in our clinical program and risks to the accuracy and usability of clinical data. As a result, our financial results and the commercial prospects for our product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed. Risks Related to Commercialization of Our Product Candidates The commercial success of ONC201, and any other product candidates, will depend upon the acceptance of these products by the medical community, including physicians, patients, pharmacists, health care payers or government agencies. Following receipt of marketing approval, a product or product candidate may not gain sufficient market acceptance by physicians, patients, healthcare payers and others in the medical community. If these products do not achieve an adequate level of market acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any of our product candidates will depend on a number of factors, including: • demonstration of clinical safety and efficacy in our clinical trials; • relative convenience, ease of administration and acceptance by physicians, patients, pharmacists and health care payers; • prevalence and severity of any AEs; • limitations or warnings contained in the FDA- approved labeling from Regulatory Authorities such as the FDA and EMA for the relevant product candidate; • availability, efficacy and safety of alternative treatments; • price and cost- effectiveness; • effectiveness of our or any future collaborators' or competitor' s sales and marketing strategies; • ability to obtain hospital formulary approval; • ability to ensure availability for product through appropriate channels; • ability to maintain adequate inventory; and • ability to obtain and maintain sufficient third- party coverage and adequate reimbursement, which may vary from country to country. Even if we obtain regulatory approval, the granting authority may still impose significant restrictions on the indicated uses, distribution or marketing of our other product candidates, including ONC201, or impose ongoing requirements for potentially costly post- approval studies or post- market surveillance. For example, the labeling ultimately approved for our product candidates, will likely include restrictions on use due to the specific patient population and manner of use in which the drug was evaluated and the safety and efficacy data obtained in those evaluations. In addition, the distribution of ONC201 may be tightly controlled through a REMS with ETASU, which are required medical interventions or other actions healthcare professionals need to execute prior to prescribing or dispensing the drug to the patient. Some actions may also be required in order for the patient to continue on treatment. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to sustainably generate revenue. We currently do not have an organization for the sales and distribution of pharmaceutical products. The cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved we must establish our sales, marketing, managerial and other non- technical capabilities or make arrangements with third parties to perform these services. We may enter into strategic partnerships with third parties to commercialize our product candidates. Our strategy for ONC201, is to establish a specialty sales force and / or collaborate with third parties to promote the product to healthcare professionals and third- party payers in the United States and elsewhere. We may elect to launch with a contract sales organization and utilize accompanying commercial support services provided by a contract sales organization. Our future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the distribution and sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that are not covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our product candidates, our ability to generate revenues from product sales, including sales of ONC201, will be adversely affected. Establishing an internal or contract sales force involves many challenges, including: • recruiting and retaining talented people; • training employees that we recruit; • establishing compliance standards; • setting the appropriate system of incentives; • managing additional headcount; • ensuring that appropriate support functions are in place to

support sales force organizational needs; and • integrating a new business unit into an existing corporate architecture. If we are unable to establish our own sales force or negotiate a strategic partnership for the commercialization of our product candidates in any markets, we may be forced to delay the potential commercialization of our product candidates in those markets, reduce the scope of our sales or marketing activities for our product candidates in those markets or undertake the commercialization activities for in those markets at our own expense. If we elect to increase our expenditures to fund commercialization activities ourselves, we will 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 will not be able to bring our product candidates to market or generate product revenue. Limited or lack of funding will impede our ability to achieve successful commercialization. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well- funded marketing and sales operations. Without an internal team or the support of a third- party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies. In addition, there are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time- consuming and could delay any product 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, marketing and market access personnel. If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business. If our product candidates are approved for commercialization, we may enter into agreements with third parties to market those product candidates outside the United States. We expect that we will be subject to additional risks related to entering into international business relationships, including: • different regulatory requirements for drug approvals in the EU and other foreign countries; • reduced protection for intellectual property rights; • unexpected changes in tariffs, trade barriers and regulatory and labor requirements; • economic weakness, including inflation, or political instability in particular foreign economies and markets; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign taxes, including withholding of payroll taxes; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; • differing payer reimbursement regimes, governmental payers or patient self- pay systems and price controls; • workforce uncertainty in countries where labor unrest is more common than in the United States; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; • regulatory risks associated with cross- border transportation of animal- sourced material; • business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters and other events outside our control including epidemics, pandemics, earthquakes, typhoons, floods and fires; and • regulatory and compliance risks that relate to maintaining accurate information and control over 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, or similar anti - bribery or anti - corruption laws and regulations. We have limited experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the EU and many of the individual countries in Europe with which we will need to comply. Many U. S.- based biopharmaceutical companies have found the process of marketing their own products outside the United States to be very challenging. We face competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively. The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical, commercial and other resources, such as larger research and development staff, stronger intellectual property portfolios and experienced marketing and manufacturing organizations and established sales forces. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, drug products that are more effective or less costly than any of our drug candidates that we are currently developing or that we may develop including ONC201. We will face competition from other drugs currently approved or that will be approved in the future for the same indications. Therefore, our ability to compete successfully will depend largely on our ability to: • discover and develop medicines that are superior to other products in the market; • demonstrate through our clinical trials that our product candidates, including ONC201, are differentiated from existing and future therapies; • attract qualified scientific, product development and commercial personnel; • obtain and successfully defend and enforce patent and / or other proprietary protection for our medicines and technologies; • obtain required regulatory approvals; • successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines; • deliver a competitive value proposition compared to established competition and / or competitors who will enter the market before or after any of our product candidates, including ONC201; and • negotiate competitive pricing and reimbursement with third- party payers. The availability of our competitors' products could affect the price we are able to charge, for any product candidate we develop. The inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects. Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in- license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or discovering, developing

and commercializing medicines before we do, which would have a material adverse impact on our business. 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. The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including: • our research methodology or that of our collaboration partners may be unsuccessful in identifying potential product candidates; • our potential 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 marketing approval; and • our collaboration partners may change their development profiles for potential product candidates or abandon a therapeutic area. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our research efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. 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 advantageous for us to retain sole development and commercialization rights. Risks Related to Our Intellectual Property If we are unable to obtain or protect intellectual property rights related to our products and product candidates, we may not be able to compete effectively in our market. We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our products and product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in- license may fail to result in issued patents with claims that cover the products in the United States or in other countries. If this were to occur, early generic competition could be expected against any product candidates we may develop. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing based on a pending patent application. Even if patents do successfully issue, third parties may challenge their validity, enforceability, scope or ownership, which may result in such patents, or our rights to such patents, being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold or license with respect to any of our product candidates fails to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found not invalid and not unenforceable, will go unthreatened by third parties or will adequately protect our products and product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market an approved product under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to any of our product candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be provoked by a third- party or instituted by us to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license it from the prevailing party, which may not be possible. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable, processes for which patents are difficult to enforce and other elements of our drug discovery and development processes that involve proprietary know- how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, that such agreements provide adequate protection and will not be breached, that our trade secrets and other confidential proprietary information will not otherwise be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If we are unable to prevent material disclosure of the non- patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Further, the laws of some foreign countries do not protect patents and other proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property abroad. We may also fail to pursue or obtain patents and other intellectual property protection relating to our products and product candidates in all foreign countries. Finally, certain of our activities and our licensors' activities have been funded, and may in the future be funded, by the U. S. federal government. When new technologies are developed with U. S. federal government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non- commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise " march- in " rights to use or allow third parties to use our patented technology. The government can exercise its march- in rights if it determines that action is necessary because we fail to achieve practical application of the U. S. government- funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U. S. industry.

In addition, U. S. government- funded inventions must be reported to the government, U. S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States. Third- party claims of intellectual property infringement may prevent or delay our development and commercialization efforts or otherwise affect our business. Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the United States Patent and Trademark Office (U. S. PTO) and its foreign counterparts. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. There may be third- party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of ONC201, or any other product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules 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 such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third- party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know- how and inventions. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our products or product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties. We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors and licensees or our other intellectual property rights, which could be expensive, time consuming and unsuccessful. Competitors **or suppliers of grey- market goods,** may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time- consuming. **We have recently initiated patent infringement proceedings in a jurisdiction outside the United States against a supplier in contravention of certain patents we own or license covering ONC201 and ONC206.** In ~~addition, in~~ an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third- party may also cause the third- party to bring counterclaims against us. We may not be able to prevent, alone or with our licensors, 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 a 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. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees on any issued patent are due to be paid to the U. S. PTO and foreign patent agencies in several stages over the

lifetime of the patent. The U. S. PTO 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. While an inadvertent 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 or our licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our product candidates, we may lose our rights and our competitors might be able to enter the market, which would have a material adverse effect on our business. Risks Related to **Our** ~~United States Government Contracts and Grants Unfavorable provisions in government contracts, may harm our business~~ **Business Operations** ~~, financial condition and operating results. United States government contracts typically contain unfavorable provisions and are subject to audit and modification by the government at its sole discretion, which will subject us to additional risks. For example, under any contract with the U. S. government, the U. S. government has the power to unilaterally: • audit and object to any contract- related costs and fees on grounds that they are not allowable under the FAR, and require us to reimburse all such costs and fees; • suspend or prevent us for a set period of time from receiving new contracts or extending our existing contract based on violations or suspected violations of laws or regulations; • claim nonexclusive, nontransferable rights to product manufactured and intellectual property developed under the contract and may, under certain circumstances, such as circumstances involving public health and safety, license such inventions to third parties without our consent; • cancel, terminate or suspend any contract based on violations or suspected violations of laws or regulations; • terminate any contract in whole or in part for the convenience of the government for any reason or no reason, including if funds become unavailable to the applicable governmental agency; • reduce the scope and value of any contract; • decline to exercise an~~ **and Industry Increasing demand** ~~option to continue any contract; • direct the course of a development program in a manner not chosen by the government contractor; • require us to perform the option segments even if doing so may cause us to forego or~~ **for compassionate** ~~delay the pursuit of other opportunities with greater commercial potential; • take actions that result in a longer development timeline than expected; and • change certain terms and conditions in any contract. The U. S. government also has the right to terminate any contract if termination is in the government' s interest, or if we default by failing to perform in accordance with the milestones set forth in the contract. Termination- for- convenience provisions generally enable us to recover only our costs incurred or committed (plus a portion of the agreed fee) and settlement expenses on the work completed prior to termination. Except for the amount of services received by the government, termination- for- default provisions do not permit recovery of fees. In addition, we must comply with numerous laws and regulations that affect how we conduct business with the United States government. Among the most significant government contracting regulations that affect our business are: • FAR, and agency- specific regulations supplements to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts and implement federal procurement policy in numerous areas, such as employment practices, protection of the environment, accuracy and retention periods of records, recording and charging of costs, treatment of laboratory animals and human subject research; • business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and incorporate other requirements such as the Anti- Kickback Act and the Foreign Corrupt Practices Act; • export and import control laws and regulations; and • laws, regulations and executive orders restricting the~~ use ~~and dissemination of information classified for~~ - **or** ~~national security purposes and the exportation of certain products and technical data. Furthermore, we may be required to enter into agreements and subcontracts with third parties, including suppliers, consultants and other~~ third- party **supply** ~~contractors, in order to satisfy our contractual obligations pursuant to our agreements with the U. S. government. Negotiating and entering into such arrangements can be time- consuming and we may not be able to reach agreement with such third parties. Any such agreement must also be compliant with the terms of our government contract. Any delay or inability to enter into such arrangements or entering into such arrangements in a manner that is non- compliant with the terms of our contract, may result in violations of our contract. As a result of these unfavorable provisions, we must undertake significant compliance activities. The diversion of resources from commercial programs to these compliance activities, as well as the exercise by the U. S. government of any rights under these provisions, could materially harm our business. Our business is subject to audit by the U. S. government and a negative audit could adversely affect our business. United States government agencies, such as the DHHS, routinely audit and investigate government contractors and recipients of federal grants. These agencies review a contractor' s performance under its contracts, cost structure and compliance with applicable laws, regulations and standards. The DHHS can also review the adequacy of, and a contractor' s compliance with, its internal control systems and policies, including the contractor' s purchasing, property, estimating, compensation and management information systems. Any costs found to be improperly allocated to a specific contract will not be reimbursed, while such costs already reimbursed must be refunded. If an audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including: • termination of contracts; • forfeiture of profits; • suspension of payments; • fines; and • suspension or prohibition from conducting business with the U. S. government. In addition, we could suffer serious reputational harm if allegations of impropriety were made against us by the U. S. government, which could adversely affect our business. In 2022, the National Institutes of Health (NIH) Division of Financial Advisory Services (DFAS) initiated a routine audit related to the BARDA development contract. This audit is a scheduled audit and not in response to any allegations of misconduct or impropriety. Risks Related to Our Business Operations and Industry Increasing demand for compassionate use~~ of our unapproved therapies could **impair or delay the completion of our controlled clinical trials or otherwise** result in losses. Recent media attention to individual patients' expanded access requests has resulted in the introduction of legislation at the local and national level

referred to as " “ Right to Try " ” laws, such as the Right to Try Act, which are intended to give patients access to unapproved therapies. New and emerging legislation regarding expanded access to unapproved drugs for life- threatening illnesses could negatively impact our business in the future. In addition, ~~during 2014,~~ we ~~were~~ **had previously been** the target of an active and disruptive social media campaign related to a request for access to TEMBEXA. If we experience similar social media campaigns in the future, we may experience significant disruption to our business which could result in losses. A possible consequence of both activism and legislation in this area is the need for us to initiate an unanticipated expanded access program or to make our product candidates more widely available sooner than anticipated. We are a small company with limited resources and unanticipated trials or access programs could result in diversion of resources from our primary goals **or may delay or prevent the regulatory approval of our products** . In addition, patients who receive access to unapproved drugs through compassionate use or expanded access programs have life- threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high which could have a negative impact on the safety profile of our product candidates, which could cause significant delays or an inability to successfully commercialize them, which could materially harm our business. Patient demand for ONC201 or ONC206 outside of our clinical trial could impair the conduct or delay the completion of our controlled clinical trials. **Currently, there are a limited number of therapeutic options available to glioma patients suffering from this severe and life- threatening disease. In the face of a glioma diagnosis, patients will often turn to alternate means of access to drug outside the scope of our current clinical trials. We are, and from time to time may be, aware of such counterfeit providers that purport to supply ONC201, ONC206 or similar versions thereof. We have taken and intend to continue taking meaningful action to eliminate such counterfeit supplies when and if appropriate. For example, we have initiated patent and trademark infringement litigation and unfair trade practice claims in a jurisdiction outside of the United States against identified sources of counterfeit supplies for ONC201 and ONC206, seeking among other things to enjoin the availability of such counterfeit supplies. These claims, and any similar actions we take, may not be successful or may take longer than anticipated to reduce or eliminate counterfeit supplies. If a significant number of patients continue to choose counterfeit supplies from third parties rather than enroll in our studies, our clinical program could be negatively impacted. In the event that patients choose to access counterfeit supplies while enrolled in our clinical studies, we may not be able to successfully meet the study endpoints and our clinical program could be negatively impacted.** We have amended the protocol of our open expanded access program to focus on patients that are not eligible for the Phase 3 ACTION ~~study~~ **Study** . Therefore, the Phase 3 ACTION ~~study~~ **Study** will serve as the main mechanism for ~~a~~ patients with newly diagnosed H3 K27M- mutant diffuse glioma following completion of radiotherapy to receive ONC201 **, apart from such counterfeit providers discussed above** . This decision could prompt adverse publicity **, could drive potential Phase 3 ACTION Study patients to seek drugs that purport to be ONC201** or **ONC206 from counterfeit providers, or cause** other disruptions related to potential participants in such expanded access programs. Competition for Phase 3 ACTION ~~study~~ **Study** eligible patients from Investigator Initiated Clinical Trials (IITs) could result in losses. We currently ~~support~~ **provide investigational product for** the Biological Medicine for Diffuse Intrinsic Pontine Glioma (DIPG) Eradication (BIOMEDE 2 **. 0**) IIT, sponsored by Gustave Roussy, in Paris **,** France. ~~It~~ **The BIOMEDE 2. 0 Study** is a multicenter, randomized open- label phase- 3 controlled trial evaluating **the** efficacy **and safety** of ONC201 **and radiation** in comparison with everolimus **and radiation** (primary objective based on internal comparison) and subsequently to historical controls. Currently, the BIOMEDE 2 **. 0** ~~study~~ **Study** is open **in France** to **pre- radiotherapy newly diagnosed H3 K27M and H3 K27me3- loss glioma** patients ~~who~~ **. Some of these patients** may be ~~otherwise~~ eligible for ~~the Phase 3 ACTION study. The competing enrollment may have a negative effect on our ability to enroll~~ the Phase 3 ACTION Study **following radiotherapy. While we believe that the impact is likely to be small in light of the small geographic footprint and limited eligibility overlap, competing enrollment could have a negative effect on our ability to enroll the Phase 3 ACTION Study** . Patients may prefer to enroll in the BIOMEDE 2 IIT instead of the Phase 3 ACTION ~~study~~ **Study** because that study does not contain a placebo control arm **, cross- over is allowed at progression, and treatment can be initiated with radiation** . Patient preference for the BIOMEDE 2 IIT could impair the conduct or delay the initiation or completion of the Phase 3 ACTION ~~study~~ **Study** . If ~~initiation or~~ completion of the Phase 3 ACTION ~~study~~ **Study** is delayed, our development costs may increase, our approval process could be delayed, any periods during which we may have the exclusive right to commercialize ONC201 may be reduced and our competitors may have more time to bring products to market before we do. Any of these events could impair our ability to generate revenues from product sales and impair our ability to generate regulatory and commercialization milestones and royalties, all of which could have a material adverse effect on our business. We ~~recently~~ **previously** worked with another IIT sponsor to amend the protocol to remove potentially Phase 3 ACTION ~~study~~ **Study** eligible patients. This decision could prompt adverse publicity or other disruptions related to potential participants in the IITs **. While the Company has negotiated a right to obtain access to the data from the BIOMEDE 2. 0 Study at a specified price should the Company desire to do so in support of a commercial authorization, there is no assurance that the Company will be able to enter into a definitive agreement** . If we fail to comply with the extensive legal and regulatory requirements affecting the health care industry, we could face increased costs, delays in the development of our product candidates, penalties and a loss of business. Our activities, and the activities of our collaborators, partners and third- party providers, are subject to extensive government regulation and oversight both in the United States and in foreign jurisdictions. The FDA and comparable agencies in other jurisdictions directly regulate many of our most critical business activities, including the conduct of preclinical and clinical studies, product manufacturing, advertising and promotion, product distribution, adverse event reporting and product risk management. States increasingly have been placing greater restrictions on the marketing practices of healthcare companies. In addition, pharmaceutical and biotechnology companies have been the target of lawsuits and investigations alleging violations of government regulations, including claims asserting submission of incorrect pricing information, impermissible off- label promotion of pharmaceutical products, payments intended to influence the referral of

federal or state healthcare business, submission of false claims for government reimbursement, antitrust violations, violations of the Foreign Corrupt Practices Act, or violations related to environmental matters. Violations of governmental regulation may be punishable by criminal, civil and administrative sanctions, including fines and civil monetary penalties and exclusion from participation in government programs, including Medicare and Medicaid. In addition to penalties for violation of laws and regulations, we could be required to delay or terminate the development of our product candidates, or we could be required to repay amounts we received from government payers, or pay additional rebates and interest if we are found to have miscalculated the pricing information we have submitted to the government. Whether or not we have complied with the law, an investigation into alleged unlawful conduct could increase our expenses, damage our reputation, divert management time and attention and adversely affect our business. Our future success depends on our ability to **manage our recent management transition,** retain key executives and to attract, retain and motivate qualified personnel. We are highly dependent on the principal members of our executive team **. Effective August 1, 2023, Michael Sherman retired from his role as President and Chief Executive Officer of the Company, and Michael Andriole, Chief Business Officer and Chief Financial Officer, was promoted to President and Chief Executive Officer. During the fourth quarter of 2024, Michelle LaSpaluto was promoted to the position of Chief Financial Officer and Thomas J. Riga was hired as Chief Operating Officer and Chief Commercial Officer of the Company. Our future performance will depend, in part, on the successful integration of these management changes. If we do not successfully manage these changes, it could be viewed negatively by our employees, investors, and other third- party partners, and could have an adverse impact on our business and results of operations** . While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are " at will " employees. To help attract, retain, and motivate qualified employees, we use share- based incentive awards such as employee stock options and restricted stock units. As of December 31, ~~2022~~ **2023** , approximately ~~95~~ **99** . ~~9~~ **5** % of all outstanding options had an exercise price above the closing price of the stock on that date. As a result, the current situation provides a considerable challenge to maintaining employee motivation, as well as creating a serious threat to retention until a recovery commences. If our share- based compensation ceases to be viewed as a valuable benefit, our ability to attract, retain, and motivate employees could be weakened, which could harm our results of operations. The share reserves under our 2013 Equity Incentive Plan (the 2013 Plan) and 2013 Employee Stock Purchase Plan (ESPP) were previously subject to automatic annual increases on January 1st of each year. ~~In the future~~ **At this time** , subject to limited exceptions, we **are** ~~will be~~ required to seek stockholder approval of future increases to the number of shares underlying our 2013 Plan (or a successor plan) and ESPP. In the event we are unable to obtain stockholder approval of such future increases, our ability to attract, retain and motivate employees through the use of share- based compensation would be substantially curtailed. We do not maintain " key person " insurance for any of our executives or other employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of appropriately skilled executives in our industry, which is likely to continue. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. In addition, failure of any of our clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee may adversely affect the progress of our research, development and commercialization objectives. 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, which could also adversely affect the progress of our research, development and commercialization objectives. Potential product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. The use of our product candidates, including ONC201, in clinical studies and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in: • impairment of our business reputation and significant negative media attention; • withdrawal of participants from our clinical studies; • significant costs to defend the related litigation; • distraction of management' s attention from our primary business; • substantial monetary awards to patients or other claimants; • inability to commercialize our product candidates, including ONC201; and • decreased demand for our product candidates, if approved for commercial sale. We currently carry $ 15 million per occurrence, and $ 15 million in the aggregate in product liability insurance covering our United States clinical trials, with additional local coverage as required for the other countries in which we conduct our trials, but not yet extending coverage to commercial sales. Our current product liability insurance coverage 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 and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may 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 stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. Risks Related ~~To~~ **to** Our Common Stock The market price of our common stock is likely to be volatile, and you may not be able to resell your shares at or above your purchase price. The trading price of our common stock has been volatile, and is

likely to continue to be volatile for the foreseeable future. Our stock price is subject to wide fluctuations in response to a variety of factors, including the following: • results of clinical trials of our product candidates or those of our competitors; • any delay in filing an application for any of our product candidates and any adverse development or perceived adverse development with respect to regulatory review of that application; • failure to successfully develop and commercialize our product candidates, including ONC201; • termination of any of our license or collaboration agreements; • developments regarding the sale of our TEMBEXA program and specified related assets to Emergent; • any agency or judicial enforcement actions against us; • inability to obtain additional funding; • regulatory or legal developments in the United States and other countries applicable to our product candidates; • adverse regulatory decisions; • changes in the structure of healthcare payment systems; • inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices; • introduction of new products, services or technologies by our competitors; • failure to meet or exceed financial projections we provide to the public; • failure to meet or exceed the estimates and projections of the investment community; • changes in the market valuations of similar companies; • market conditions in the pharmaceutical and biotechnology sectors, and the issuance of new or changed securities analysts' reports or recommendations; • announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors; • significant lawsuits (including patent or stockholder litigation), and disputes or other developments relating to proprietary rights (including patents, litigation matters and our ability to obtain patent protection for our technologies); • additions or departures of key scientific or management personnel; • sales of our common stock by us or our stockholders in the future; • trading volume of our common stock; • general economic, industry and market conditions ~~, including the impact of the ongoing COVID- 19 pandemic~~ ; and • the other factors described in this " Risk Factors " section. In addition, the stock market in general, and The Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. Based upon shares of common stock outstanding as of December 31, ~~2022~~ **2023** , our then executive officers, directors, 5 % stockholders (known to us through available information) and their affiliates beneficially owned approximately ~~30~~ **28** . ~~8~~ **9** % of our voting stock. Therefore, these stockholders have the ability to substantially influence us through this ownership position. For example, these stockholders, if they choose to act together, may be able to influence the election of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire. ~~Shareholder activism could cause material disruption to our business. Publicly traded companies have increasingly become subject to campaigns by activist investors advocating corporate actions such as actions related to financial restructuring, dividends, share repurchases and even sales of assets or the entire company. For example, our shareholder Rubric Capital Management (Rubric) issued a press release and filed a Schedule 13D in November 2022, in which Rubric expressed a lack of confidence in the Company' s strategic direction. In response, the Company issued a press release in which we stated we do not believe a liquidation of the Company is in the best interests of all of our shareholders as it would deprive them of the significant upside potential of ONC201 and our other assets. We also stated it would be irresponsible to patients with this deadly disease as it would halt critical progress on ONC201. We stated we are confident that the continued successful execution of our strategy is the best path to maximize shareholder value, and that our Board and leadership team regularly consider all opportunities to create or enhance value. Responding to proxy contests and other actions by Rubric or other activist investors could be costly and time- consuming, disrupt our operations and divert the attention of our board of directors and senior management from the pursuit of our business strategies, which could adversely affect our results of operations and financial condition.~~ Failure to establish and maintain adequate finance infrastructure and accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies. As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes- Oxley Act of 2002, and the related rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes- Oxley Act include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. Our compliance with Section 404 of the Sarbanes- Oxley Act has required and will continue to require that we incur substantial accounting expense and expend significant management efforts. In this or future years, our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner so as to be able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act each year. If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act in a timely manner each year, we could be subject to sanctions or investigations by the Securities and Exchange Commission, The Nasdaq ~~Stock~~ **Global** Market or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information. Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing 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. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. We are continuing to review additional potential transactions to add to our pipeline of product candidates, and these transactions could involve the issuance of additional shares of common stock or other equity securities. For example, on January 7, 2021, we acquired Oncoceutics, a privately- held, clinical- stage biotechnology company developing imipridones, including ONC201. As part of the consideration for the acquisition, we paid an upfront cash payment of approximately $ 25. 0 million and issued an aggregate of 8, 723, 769 shares of our common stock. Pursuant to ~~our 2013 Equity Incentive Plan (~~ the 2013 Plan ~~)~~, our management is authorized to grant stock options to our employees, directors and consultants. In addition, our board of directors may grant or provide for the grant of rights to purchase shares of our common stock pursuant to the terms of our 2013 Employee Stock Purchase Plan (ESPP). To the extent we seek, and our stockholders approve, future increases to the number of shares underlying our 2013 Plan (or a successor plan) and ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall. We have broad discretion in the use of the net proceeds from our financing transactions and may not use them effectively. Our management has broad discretion in the application of the net proceeds from our financing transactions. Because of the number and variability of factors that will determine our use of the net proceeds from our financing transactions, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we have invested the net proceeds from our financing transactions in investment- grade, interest- bearing securities with maturities less than 24 months. These investments may not yield a favorable return to our stockholders. Volatility in our stock price could subject us to securities class action litigation. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations. New tax laws, statutes, rules, regulations or ordinances could be enacted at any time. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted differently, changed, or modified. Any such enactment, interpretation, change or modification could adversely affect us, possibly with retroactive effect. For example, the ~~recently enacted~~ IRA imposes, among other rules, a 15 % minimum tax on the book income of certain large corporations and a 1 % excise tax on certain corporate stock repurchases. **In addition, for certain research and experimental expenses incurred in tax years beginning after December 31, 2021, the Tax Cuts and Jobs Act (the Tax Act) requires the capitalization and amortization of such expenses over five years if incurred in the United States and fifteen years if incurred outside the United States, rather than deducting such expenses currently. There have been legislative proposals to repeal or defer the research and experimental expense capitalization rules, including legislation recently passed by the U. S. House of Representatives that would restore the deductibility of U. S. based research and experimental expenses but not non- U. S. research and experimental expenses, but there can be no assurance that any such legislation will ultimately be enacted** . Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act as amended by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) or any future tax reform legislation, could have a material impact on the value of our deferred tax assets, could result in significant one- time charges, and could increase our future U. S. tax expense. Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts. Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the Tax Act, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. ~~Our federal~~ **As of December 31, 2023, we had** net operating loss (NOL) carryforwards **of $ 423. 2 million and $ 416. 0 million available to reduce future taxable income, if any, for U. S. federal income tax and state income tax purposes, respectively. Our federal NOLs** generated in tax years beginning before January 1, 2018, are only permitted to be carried forward for 20 years under applicable U. S. tax law **. If not utilized, our federal and state NOL carryforwards begin to expire in 2035 and 2024, respectively. Portions of these NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities** . Under the Tax Act, as amended by the CARES Act, our federal NOLs generated in tax years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the Tax Act or the CARES Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is generally defined as a greater than 50 % change, by value, in its equity ownership over a three- year period, the corporation' s ability to use its pre-change NOL carryforwards and certain other pre- change federal tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our federal carryforwards and certain other pre- change federal tax attributes (such as research tax credits) to offset our post- change income or taxes could be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited. As a result, we may

be unable to use all or a material portion of our state NOL carryforwards and other state tax attributes, which could accelerate or permanently increase state taxes owed. Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be your sole source of gain. We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain any future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future. Provisions in our corporate charter documents and under Delaware law could make it more difficult for a third- party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders and may prevent attempts by our stockholders to replace or remove our current management. Some provisions of our charter documents and Delaware law may have anti- takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include: • authorizing the issuance of " blank check " preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval which could be used to institute a " poison pill " that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; • allowing the authorized number of our directors to be changed only by resolution of our board of directors; • limiting the removal of directors; • creating a staggered board of directors; • requiring that stockholder actions must be effected at a duly called stockholder meeting and prohibiting stockholder actions by written consent; • eliminating the ability of stockholders to call a special meeting of stockholders; and • establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at duly called stockholder meetings. The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require the affirmative vote of the holders of at least 66 2 / 3 percent of the voting power of all of our then outstanding common stock. 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, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us. Risks Related to **Data Privacy We are subject to stringent and evolving U. S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences. We process personal data and other sensitive information, which subjects us to numerous evolving data privacy and security obligations. In the ordinary course of business, we collect, receive, store, process, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive information, including proprietary and confidential business data, intellectual property, data we collect about trial participants in connection with clinical trials, sensitive third- party data, and other sensitive data. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act), and other similar laws (e. g., wiretapping laws). For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. In the past few years, numerous U. S. states — including California, Virginia, Colorado, Connecticut, and Utah — have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt- out of certain data processing activities, such as targeted advertising, profiling, and automated decision- making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 (CCPA), as amended by the California Privacy Rights Act of 2020 (CPRA) (collectively, CCPA) applies to personal information of consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA provides for fines of up to $ 7, 500 per intentional violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Similar laws are being considered in several other states, as well as at the federal and local levels. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely. Outside the United States, an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, we are subject to the European Union' s General Data Protection Regulation (EU GDPR) and the United Kingdom' s GDPR (UK**

GDPR) (collectively, GDPR). Under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the GDPR / 17. 5 million pounds sterling under the UK GDPR, or 4 % of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The Swiss Federal Act on Data Protection (FADP) also applies to the collection and processing of personal data, including health- related information, by companies located in Switzerland, or in certain circumstances, by companies located outside of Switzerland. In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA), Switzerland, and the United Kingdom have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross- border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA, Switzerland, and United Kingdom to the United States in compliance with law, such as the EEA standard contractual clauses, the United Kingdom' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the United Kingdom extension thereto (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, Switzerland, the United Kingdom or other jurisdictions to the United States, or if the requirements for a legally- compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA, Switzerland, and United Kingdom to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR' s cross- border data transfer limitations. Obligations related to data privacy and security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources, which may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e. g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class- action claims) and mass arbitration demands; additional reporting requirements and / or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: interruptions or stoppages in our business operations (including our clinical trials); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations. Risks Related to Information Technology **If our** ~~Significant disruptions of~~ information technology systems or ~~breaches of~~ data ~~security~~ **, or those of third parties upon which we rely, are or were compromised, we** could **experience** ~~adversely-~~ **adverse** ~~affect~~ **consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of** our business **operations; reputational harm; loss of revenue or profits; and other adverse consequences** . ~~Our~~ **In the ordinary course of our** business ~~is increasingly dependent on critical~~ , **we** ~~complex,~~ and ~~interdependent~~ **the third parties upon which we rely, process proprietary, confidential, and sensitive data, including personal data (such as health- related data), intellectual property, trade secrets and any other sensitive data. Cyber- attacks, malicious internet- based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and** information technology **systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer " hackers, " threat actors, " hacktivists, " organized criminal threat actors, personnel** (~~IT~~ **such as through theft or misuse**) **, sophisticated nation states, and nation- state- supported actors. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, which could materially disrupt our** systems **and operations, supply chain, and ability to produce, sell and distribute our goods and services. We and the third parties upon which we rely are subject to a variety of evolving threats** , including ~~Internet~~ **but not limited to social- engineering attacks (including through deep fakes, which may be increasingly more difficult to**

identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks, credential stuffing attacks), credential harvesting, personnel misconduct or error, ransomware attacks, supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, telecommunications failures, earthquakes, fires, floods, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We rely on third- party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation clinical trial data processing, cloud - based ~~systems~~ **infrastructure , data center facilities, encryption** ~~to support business processes as well as internal~~ and ~~external communications. The size~~ **authentication technology, employee email,** and ~~complexity of~~ **other functions. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third- party service providers experience a security incident** ~~our~~ **or** ~~IT systems make~~ **other interruption, we could experience adverse consequences. While we may be entitled to damages if our third- party service providers fail to satisfy their privacy or security- related obligations to** us ~~potentially vulnerable to IT system breakdowns~~ , **any award** ~~malicious intrusion, and computer viruses, which~~ may ~~result in the impairment of~~ **be insufficient to cover our damages,** ~~our~~ **or** ~~ability~~ **we may be unable** to **recover such award** ~~operate our business effectively~~ . In addition, **supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain** ~~our~~ **or our third- party partners' supply chains have not been compromised. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate, and remediate such vulnerabilities in our information** systems **(such as our hardware and / or software, including that of third parties upon which we rely). We may not, however, be able to detect and remediate all vulnerabilities, including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our products. We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures or industry- standard or reasonable security measures to protect our information technology systems and sensitive information. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents, including affected individuals, customers, regulators, and investors. Such disclosures** are **costly, and the disclosure** ~~potentially vulnerable to data security breaches- whether by employees~~ or **the failure** ~~others- which may expose sensitive data~~ to **comply with** ~~unauthorized persons. Such~~ **such requirements** ~~data security breaches~~ could lead to ~~the loss of trade secrets~~ **adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (** ~~or~~ **for example** ~~other intellectual property~~ **, investigations, fines, penalties, audits, and inspections); additional reporting requirements and /** or **oversight; restrictions on processing sensitive** ~~could lead to the public exposure of personal~~ information (including ~~sensitive~~ personal ~~information~~ **data**) **; litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; diversion** of **management' s attention; interruptions in** our ~~employees, clinical trial patients, customers, business partners~~ **operations (including availability of data); financial loss;** and ~~others~~ **other similar harms** . ~~Any~~ **Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that** such ~~disruption~~ **coverage will continue to be available on commercially reasonable terms** or **at all** ~~security breach could result in legal proceedings~~ , **or** ~~liability under laws~~ that **such coverage will pay future claims** ~~protect the privacy of personal information, regulatory penalties, disruptions to our operations and collaborations, and damage to our reputation, which could harm our business and results of operations~~ . Increasing use of social media could give rise to liability, breaches of data security, or reputational damage. 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 products or business may cause us to be found in violation of applicable laws and regulations. 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 products in social media could seriously damage our reputation, brand image, and goodwill. ~~49~~