Risk Factors Comparison 2024-03-18 to 2023-03-27 Form: 10-K

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

Any one or more of these risks, if realized, could reduce or eliminate future revenue from product candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations and / or growth prospects. We contract with **a limited number of** third parties for the manufacture of our product candidates for preclinical development **and clinical testing** and expect to continue to do so for clinical testing and commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our products if any of our product candidates receive regulatory approval. In some cases, we rely on one party **or two parties** to manufacture our preclinical and clinical products and we exercise limited direct control over ~~this~~ **these** ~~manufacturer~~ **manufacturers** (and it would be time consuming and expensive to move production to ~~a~~ **any** new ~~manufacturer~~ **manufacturers** , if we were able to do so at all). This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. ~~For example, we rely on a limited number of CDMOs to perform certain chemistry- related work on our preclinical product candidates. One such CDMO is located in Ukraine, which was invaded by Russia in February 2022 and, as a result, their work on our behalf of was interrupted. Another CDMO, with operations in Shanghai, was impacted when lock- down procedures were recently implemented due to COVID- 19 and was unable to operate at full capacity. Events such as those in Ukraine and China may delay development of our future product candidates, which have been temporary and limited to date, but such delays may materially impact the timing for moving products into development candidate stage and IND- enabling studies, as well as initiating trials, in the future.~~ The facilities used by our contract manufacturers to manufacture our product candidates must be inspected by the FDA pursuant to pre- approval inspections that will be conducted after we submit our ~~marketing~~ **NDA** applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMP in connection with the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or ~~others~~ - **other regulatory agencies** , they will not be able to pass regulatory inspections and / or maintain regulatory compliance for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory ~~authority~~ **agency** finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it finds deficiencies or withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. If any CDMO with whom we contract fails to perform its obligations, we may be forced to enter into an agreement with a different CDMO, which we may not be able to do on reasonable terms, ~~if~~ **or** at all, and such new agreement may result in significantly greater costs to us. In such scenario, our **supply of study drug for** clinical trials ~~supply~~ could be **disrupted or** delayed significantly as we establish alternative supply sources. In some cases, the technical skills **or processes** required to manufacture our products or product candidates may be unique or proprietary to the original CDMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills **or processes** to a back- up or alternate supplier, or we may be unable to transfer such skills **or processes** at all. In addition, if we are required to change CDMOs for any reason, we will be required to verify that the new CDMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory ~~authority~~ **agency** . The delays associated with the verification of a new CDMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CDMO may possess technology related to the manufacture of our product candidate that such CDMO owns independently. This would increase our reliance on such CDMO or require us to obtain a license from such CDMO in order to have another CDMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Further, our failure, or the failure of our third- party manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our product candidates. Our product candidates and any products that we may develop may compete with other product candidates and approved products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. The third parties upon whom we rely for the supply of the active pharmaceutical ingredients and drug product to be used in our product candidates are our sole ~~source~~ **sources** of supply, and the loss of any of these suppliers could significantly harm our business. The active

pharmaceutical ingredients, or API, ~~and drug product~~ we ~~expect~~ **use and that we may continue** to use in all of our product candidates are supplied to us from **one** ~~single- source suppliers~~ **supplier. The** ~~, in some cases the same manufacturer produces the API and~~ drug product **used in our product candidates is supplied by two manufacturers (and the manufacturer that produces the API is also one of the two suppliers of our the drug product used in our current clinical trials)** . Our ability to successfully develop our product candidates, and to ultimately supply our commercial products in quantities **(if approved by regulatory authorities)** sufficient to meet the market demand (and to meet requirements in connection with our **ongoing and** planned clinical trials), depends in part on our ability to obtain the API and drug product for these products in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. We are also unable to predict how changing global economic conditions or global health concerns ~~such as the ongoing COVID- 19 pandemic~~ , as well as potential supply chain disruptions or cost increases related thereto, will affect our third- party suppliers and manufacturers. **The risk related to global economic and political changes and supply chain disruption could have a material impact since one of our two CDMOs is located in China. Further, this CDMO, which is our sole supplier of API for the drugs used in our clinical trials, is affiliated with WuXi AppTec, and WuXi AppTec has been the subject of a recent proposed Congressional legislation that, if approved or if the subject of executive or administrative action, could restrict WuXi' s business in the United States or the ability of businesses in the United States to conduct business with WuXi (on national security grounds). We have started the process to locate an alternate producer of API, but there is no guarantee that we can identify and engage an alternate producer or manufacturer in time so as not to disrupt our trials, on terms that are acceptable to us (including financial terms), or at all.** Any negative impact of ~~such matters on~~ **the ability of our CDMOs to deliver drug substance and drug product, due to political actions, supply chain disruption** ~~our~~ **or otherwise,** ~~third- party suppliers and manufacturers~~ may ~~also~~ have an adverse impact on our results of operations or financial condition. For all of our product candidates, we intend to identify and qualify additional manufacturers to provide such API and drug product prior to submission of an NDA to the FDA and / or an MAA to the EMA. We are not certain, however, that our single- source suppliers **or limited number of suppliers** will be able to meet our demand for products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for ~~their~~ products on a timely basis in the past, they may subordinate our needs in the future to their other customers **or may experience operating disruptions** . Establishing additional or replacement suppliers for the API and drug product used in our product candidates **and clinical trials** , if required, may not be accomplished quickly (or at all). If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay. While we seek to maintain adequate inventory of the API and drug product used in our product candidates **and clinical trials** , any interruption or delay in the supply of components or materials, or our inability to obtain such API and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects. Risks Related to Our Intellectual Property If we cannot obtain new patents, maintain our existing patents and protect the confidentiality and proprietary nature of our trade secrets and other intellectual property, our business and competitive position may be harmed. Our success depends in part on our ability to obtain and maintain patent and regulatory protections for our products candidates, to preserve our trade secrets and other proprietary rights and to prevent third parties from infringing on our rights and our proprietary technology. We have procured patent rights, through both ownership and license, that cover our product candidates, and expect **to** apply for additional patent protections in the future. However, our patent applications may not result in the issuance of patents in the U. S. or other countries. In addition, a patent may be issued in one country, but a counterpart patent may not be issued in another country, which is not uncommon in the biopharmaceutical industry **. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign countries may require the payment of maintenance fees or patent annuities during the lifetime of a patent application and / or any subsequent patent that issues from the application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. 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. Such noncompliance can result in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance 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. Such an event could have a material adverse effect on our business** . Even if a patent is issued, that is not conclusive as to its inventorship, scope, validity or enforceability and therefore that patent may not afford adequate (or any) protection for our product candidates or future approved products. On the basis of such inconclusiveness, third parties may challenge our patents. Furthermore, patents have a limited lifespan. In the United States and most other jurisdictions in which we have undertaken patent filings, the natural expiration of a patent is generally twenty years after it is filed, assuming all maintenance fees are paid. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, patents we may own or in- license may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our current or future product candidates, including generic versions of ~~such~~ **our** drugs. Nor can we be certain that we will obtain any patent term extension as permitted under the " Hatch- Waxman Amendments " which permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. If any of our patents are narrowed, invalidated, revoked or

become unenforceable, competitors may develop and market products similar or identical to ours that do not conflict with or infringe our patents rights, which could have a material adverse effect on our financial condition. Even if we obtain and maintain patents, our business may be significantly harmed if the patents are not broad enough to protect our products from copycat or similar products. In addition, if there are challenges to our intellectual property by third parties, we may in the future enter into agreements with those parties that provide certain intellectual property rights to our future marketed products or products in our pipeline. If we do enter into such agreements, we may not be the exclusive provider of a therapy and, as a result, we expect that any potential revenue from the sales of such therapies would be materially and negatively impacted. We may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to **or were involved in generating** our proprietary know- how, information or technology to assign or grant similar rights to the inventions they make in the course of their work to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. We have, and expect that we will continue, to finance or collaborate in research and development projects conducted by third parties, including government organizations, hospitals, universities or other educational or research institutions, or other for- profit companies. Such third parties may be unwilling to grant us certain rights to technology or products developed through such projects. **Certain collaborators may only grant us a right to obtain a license to technology developed in a collaboration, and we may not be able to negotiate a license or the license may require an upfront or royalty payment.** Disputes may also arise as to the rights to technology or products developed in collaboration with such third parties and we may not be able to secure the proprietary rights to any technology generated in such collaboration. Significant legal questions exist concerning the extent and scope of patent protection for biopharmaceutical products and processes in the U. S. and elsewhere. Accordingly, there is no certainty that patent applications owned or licensed by us will issue as patents, or that our issued patents will afford meaningful protection against competitors. Once issued, patents are subject to challenge through both administrative and judicial proceedings in the U. S. and **certain** other countries. Such proceedings include re- examinations, inter partes reviews, post- grant reviews and interference proceedings before the U. S. Patent and Trademark Office, as well as opposition proceedings before the European Patent Office and other non- U. S. patent offices. Certain countries have laws that provide stronger bases for challenging third party patent rights than are available to challenge patents in other countries. Therefore, we may be able to defend our patents against a third- party claim in one country but counterpart patents may be invalidated in other countries and we may be able to invalidate a third- party patent in one country but not invalidate its counterpart patents in other countries. Further, ~~,~~in jurisdictions outside the United States, a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Accordingly, any actual or purported co- owner of our patent rights could seek monetary or equitable relief requiring us to pay it compensation for, or refrain from, exploiting these patents due to such co- ownership. Litigation may be required to enforce, defend or obtain our patent and other intellectual property rights. Any administrative proceeding or litigation could require a significant commitment of our resources and, depending on outcome, could adversely affect the scope, validity or enforceability of certain of our patent or other proprietary rights. Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same compounds, methods, formulations or other subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until at least 18 months after the earliest priority date of patent filing, or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in patents we may own or in- license patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. Some of the sensitive technology, techniques and proprietary compounds used in our business are protected as trade secrets. Among other things, we enter into confidentiality agreements and license agreements to protect proprietary know- how that may not be patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know- how, information, or technology that may not be covered by patents (or for which we determine we will not seek patent protection). Although we seek to require 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, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information (or that the terms of such agreements are enforceable). In our business, we rely on collaboration with, or discuss the potential for collaboration with, suppliers, outside scientists **, research organizations** and other biopharmaceutical companies. Collaboration and discussion of potential collaboration or inadvertent disclosure of a trade secret present a strong risk of exposing our trade secrets. If our trade secrets were exposed, we may lose the protection and potential exclusive rights afforded by trade secret law, and such exposure may likely help our competitors and allow them to access technology without restriction and adversely affect our business prospects. In addition, the patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. **In some instances, a delay in filing patent applications could adversely impact patentability, for example if certain information is disclosed prior to the filing of a patent application. Under certain circumstances, use of the compounds in clinical trials could be**

interpreted as a public use and negatively impact our ability to obtain patent protection for certain inventions. Due to expense of patent filings, we also may not file in every jurisdiction in which patents may be issued (and, therefore, we may not be able to assert patents rights in every country in the future). Further, with respect to certain pending patent applications covering our current or future product candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office (s) may be significantly narrowed by the time they issue, if they ever do. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license **or access** from or to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Similarly, trademarks and trade names we utilize in our business may be challenged, infringed, diluted or declared generic or determined to be infringing on other marks. These marks can be important for name recognition in markets. If we are unable to secure and protect our trademarks and trade names, our business could be harmed. If we are found to be infringing third party patents, we may be forced to pay damages to the patent owner and / or obtain a license to continue the manufacture, sale or development of our products. If we cannot obtain a license, we may be prevented from the manufacture, sale or development of our products or product candidates, which may adversely affect our business. Parts of our technology, techniques, proprietary compounds and potential product candidates, including those which are or may be in- licensed or developed in collaboration with third parties, may be found to infringe patents owned by or granted to others. We may in the future receive notices claiming our products (if approved) and product candidates infringe third party patents (and **we have received and may in the future receive** notices offering the right to license certain technology to us) and third parties may in the future file civil lawsuits against us claiming infringement of their intellectual property rights. Third parties may claim that the manufacture, use or sale of our products or product candidates infringes patents owned or granted to such third parties. We may become aware of patents owned by third parties that might be claimed by such third parties to be infringed by the development **, use, manufacture** and commercialization of our products (if approved) or our investigational compounds. In such cases we may take certain actions with respect to some of these, for example we may try to invalidate the **third- party** patents or obtain licenses to a technology or invention. Any holder of patents covering similar **or identical** technology to our technology could sue us for damages, which may be material in amount, and seek to prevent us from manufacturing, selling or developing our products (and we may be, in certain cases, prevented from initiating product launches in certain jurisdictions or **be** required to withdraw the product from the market after it has been launched). Intellectual property disputes ~~,~~ can be costly and time consuming to defend and there is no guarantee that we would prevail in such lawsuit. If we **believe we** cannot successfully defend against ~~any~~ **certain** infringement claims, we may seek to invalidate the patent or seek a license to the technology prior to or during legal actions in order to reduce the risks in connection with the product launches (or at a later time after product introduction) and to reduce further costs and the risk of a court determination that our technology, techniques, proprietary compounds or potential product candidates infringe the third party' s patents. A required license may be costly or may not be available on acceptable terms, if at all. A costly license, or inability to obtain a necessary license, could have a material adverse effect on our business. In some instances, we believe we may prevail in a patent infringement action. There can, however, be no assurance that the court will agree with our position or that it will decide any infringement case in our favor. Nor can we be certain that, if we do not prevail in litigation, that we may be able to obtain a license to any third- party patent on commercially reasonable terms (or at all); successfully develop non- infringing alternatives on a timely basis (or at all); or license alternative non- infringing technology, if any exists, on commercially reasonable terms (or at all). Any impediment to our ability to manufacture, use or sell approved forms of our future products (if approved by regulatory authorities) or our product candidates could have a material adverse effect on our business and prospects. It is possible that we could lose market exclusivity for a product earlier than expected, which may harm our competitive position. In our industry, much of an innovative product' s commercial value is realized while it has market exclusivity. Market exclusivity for our future products (if approved for sale by regulatory authorities) will likely depend in large part on patent rights and certain regulatory forms of protection. As noted above, patent protection can be uncertain as to the validity, scope and enforceability of many issued patents. Absent relevant patent protection for a product, once regulatory exclusivity periods expire, generic versions of the product can be approved and marketed. The market exclusivity of our products may be impacted by competitive products that are either innovative or generic copies. In our industry, the risk of generic challenges has been increasing. U. S. law includes an approval pathway for generic versions of innovative small molecule products. Under the pathway, the FDA may approve products that are generic copies of innovative small molecule therapies on the basis of less extensive data than is required for a full new drug application. The law provides a mechanism to challenge the patents that protect an innovator' s products. Such litigation may begin as early as four years after the innovative small **molecule** product is first approved by the FDA. Pathways for generic products also exist in many other markets, including Europe and Japan. Competition, including from generics approved for marketing, would likely result in a decrease in volume of sales of our products, as well as a decrease in prices and lower margins for our products (if approved for marketing by regulatory authorities). We may initiate, become a defendant in, or otherwise become party to lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming, and unsuccessful. Competitors may infringe any patents we may own or in- license, our trade secrets or other proprietary rights. In addition, any patents or other proprietary rights we may own or in- license also may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming **to litigate** . We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful (and we may not be able to prevent the commercialization of ~~the~~ **any** competitor product **or a generic**). In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in- license is not valid or is unenforceable or that the other party' s

use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U. S. C. § 271 (e) (1 **) (relating to conduct used in connection with obtaining regulatory approval of a medical device or drug**). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any patents we may own or in- license do not cover the technology in question or that such third party' s activities do not infringe our patent applications or any patents we may own or in- license (or any other proprietary rights we may own). An adverse result in any litigation or defense proceedings could put one or more of any patents we may own or in- license at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings relating to our proprietary rights could have a material adverse effect on our ability to compete in the marketplace and may negatively impact our stock price. Post- grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patent applications or any patents we may own or in- license. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights (or technology covered under current patent applications) and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms **, or at all** . In addition to potential USPTO post- grant proceedings, we may become a party to patent opposition proceedings in the EPO, or similar proceedings in other foreign patent offices or courts where our patents may be challenged. The costs of these proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. Even in cases in which we or our licensors or strategic partners initiate legal proceedings against a third party to enforce a patent covering one of our current or future product candidates, the defendant could (and in pharmaceutical patent litigation the defendant often does) make a counterclaim that the patent covering our product candidate, as applicable, is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. If such counterclaims are successful, the exclusivity related to the product may be lost and our business would be harmed. Intellectual property litigation and administrative patent office patent validity challenges in one or more countries could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could ` distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for research and development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately **(and we may decline to initiate litigation against a potential infringing party because the cost of the litigation and use of cash resources may be determined to not be in the best interests of the company at such time).** We may be subject to damages or settlement costs resulting from claims that we or our employees have violated the intellectual property rights of third parties, or are in breach of our agreements. We may be accused of, allege or otherwise become party to lawsuits or disputes alleging wrongful disclosure of third- party confidential information by us or by another party, including current or former employees, contractors or consultants. In addition to diverting attention and resources to such disputes, such disputes could adversely impact our business reputation and / or protection of our proprietary technology. The intellectual property landscape relevant to our product candidates and programs is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on **our results of operations and** the success of our business. We cannot assure you that our current or future product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. For example, many of our employees were previously employed at other biotechnology or pharmaceutical companies **or research institutions** . Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s former employer. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more of our current or future product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to: ? substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party' s rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner' s attorneys' fees; ? a court prohibiting us from developing, manufacturing, marketing or selling our current product ~~candidate~~ **candidates** , including TNG908 ~~and~~ **,** TNG462, **TNG260 or TNG348** or future product candidates, or from using our proprietary technologies, unless the third party licenses its product **, process or other** rights to us, which it is not required to do, on commercially reasonable terms or at all; ? if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and / or grant cross- licenses to intellectual property rights for our products **, processes or other rights** , or the license to us may be non- exclusive, which would permit third parties to use the same intellectual property to compete with us; ? redesigning our current or future product candidates or processes so they do not infringe, misappropriate or violate third- party intellectual property rights, which may not be possible or may require substantial

monetary expenditures and time; and ? there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. We may be unable to obtain patent or other intellectual property protection for our current or future product candidates or our future products, if any, in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek **or obtain intellectual property** protection. We may not be able to **(or we may decide not to)** pursue patent coverage of our current or future product candidates **and technologies** in all countries. Filing, prosecuting and defending patents on current or future product candidates **and technologies** in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where intellectual property rights enforcement is not as strong as that in the United States. These products may compete with our current or future product candidates and in jurisdictions where we do not have any issued patents our patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Much of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to pharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in- license or marketing of competing products in violation of our proprietary rights generally. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents we may own or license that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. **Our European patents and patent applications could be challenged in the recently created Unified Patent Court, or UPC, for the European Union. We may decide to opt out of our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non- compliance and brought under the jurisdiction of the UPC. We cannot be certain that our European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. A successful invalidity challenge to a European patent under the UPC would result in loss of patent protection in those European countries. Accordingly, a single proceeding under the UPC could result in the partial or complete loss of patent protection in numerous European countries, rather than in each validated European country separately as such patents have historically been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.** If we fail to comply with our obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We may from time to time be party to license and collaboration agreements with third parties to advance our research or allow commercialization of current or future product candidates. For example, in March 2020 we entered into a License Agreement with Medivir with respect to certain technology related to USP1. Such agreements may impose numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements. Further, the terms of these agreements can be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business **.** Any termination of these licenses, or if the underlying patents **or intellectual property or proprietary rights** fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our current or future product candidates, and competitors or other third parties

would have the freedom to seek regulatory approval of, and to market, products identical **or similar** to ours and we may be required to cease our development and commercialization of certain of our current or future product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including: ? the scope of rights granted under the license agreement and other interpretation- related issues; ? whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement; ? our right to sublicense patent and other rights to third parties under collaborative development relationships; ? our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our current or future product candidates, and what activities satisfy those diligence obligations; ? the priority of invention of any patented technology; and ? the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners **and collaborators** . Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our current or future product candidates. Patent reform legislation in the United States and other countries, including the Leahy- Smith America Invents Act, or Leahy- Smith Act, signed into law on September 16, 2011, could increase uncertainties of the scope of our patent protection and the costs related to obtaining and enforcing our patents. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. In addition, the Leahy- Smith Act has transformed the U. S. patent system into a " first inventor to file " system. The first- inventor- to- file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U. S. Congress, the U. S. courts, the USPTO and the relevant law- making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our rights under patents that we might obtain in the future. Further, other countries and jurisdictions, such as the European Union, periodically review their intellectual property laws and they may also take similar actions that impact the laws and regulations governing patents and they may implement changes that could weaken our ability to obtain new patents or to enforce our rights under patents that we might obtain in the future **.** We may not identify relevant third- party patents or may incorrectly interpret the relevance, scope or expiration of a third- party patent, which might subject us to infringement claims or adversely affect our ability to develop and market our current or future product candidates. We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third- party patent and pending patent application in the United States and abroad that is relevant to or necessary for the commercialization of our current or future product candidates in any jurisdiction. For example, U. S. patent applications filed before November 29, 2000 and certain U. S. patent applications filed after that date that will not be filed outside the United States remain confidential until patents issue. As mentioned above, patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our current or future product candidates could have been filed by third parties without our knowledge. Additionally, identification of third- party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to, for example, differences in terminology among patents or incomplete databases. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future product candidates or **technologies or** the use of our current or future product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our current or future product candidates **or use certain technologies** . We may incorrectly determine that our current or future product candidates **or technologies** are not covered by a third- party patent or may incorrectly predict whether a third party' s pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our current or future product candidates **or use certain technologies** . Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our current or future product candidates **or use certain technologies** . If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully

settle or otherwise resolve such infringement claims which can result in the adverse consequences related to infringement as described in the preceding risk factors. Intellectual property rights do not guarantee commercial success of current or future product candidates or other business activities. Numerous factors may limit any potential competitive advantage provided by our intellectual property rights. The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain ~~our~~ **any** competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative: ? patents, should they issue, that we may own or in- license, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable; ? others may be able to develop and / or practice technology, including compounds that are similar to the chemical compositions of our current or future product candidates, that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in- license, should any patents issue; ? we, or our future licensors or collaborators, might not have been the first to make the inventions or to file the patent covered by a patent application that we own or may in- license; ? others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights; ? our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets; ? we may choose not to file a patent in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent covering such trade secrets or know- how; ? we may not be able to maintain the confidentiality of our trade secrets or other proprietary information; ? we may not develop or in- license additional proprietary technologies that are patentable; and ? the patents of others may have an adverse effect on our business. Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects. Risks Related to Government Regulation Our future commercial success depends on gaining regulatory approval for new products and obtaining approvals for new indications. We invest significant amounts in developing new products and technologies. Our success and revenue growth, if any, will depend in part on our identification, development and commercialization of new products and technologies, and approval of additional indications for our any products under development. Product development is very expensive, takes significant time and involves a high degree of risk. Only a small number of research and development programs result in the commercialization of a product. Our ability to grow our business may be adversely affected if we are delayed or unable to successfully develop the products in our pipeline, if we are unable to gain regulatory approval of such product candidates, and expand the indications that may be treated by such product candidates, and gaining regulatory approval to sell and market such product candidates in additional jurisdictions. We must also maintain all such regulatory approvals for the period of time that we sell the product in each such jurisdiction. Our failure to obtain, or a delay in obtaining, approval or our failure to maintain approvals once obtained, will prevent us from selling products and generating revenues for those products in such jurisdiction where we do not hold such approvals **.** Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Assuming that our product candidates prove to be safe and effective in clinical trials, we expect that we will file for marketing approval for such product candidates in the United States and we may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and / or fail to receive applicable regulatory approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and future potential revenue may be less than expected by investors and analysts. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants regulatory approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, **sale,** marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In short, the foreign regulatory approval process involves all of the risks associated with FDA approval. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we may intend to charge for our products will also be subject to approval. We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process. If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months from the date of filing, rather than the standard review period of ten months **from the date of filing** . We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation

does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six- month review cycle or at all. We may seek orphan drug designation for certain of our product candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity. As part of our business strategy, we may seek orphan drug designation for certain of our product candidates, and we may be unsuccessful **in obtaining such designation** . Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals annually in the United States, or a patient population of 200, 000 or more in the United States where there is no reasonable expectation that the cost of developing the product will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user- fee waivers. The FDA granted Orphan Drug Designation to TNG908 for the treatment of malignant peripheral nerve sheath tumors (MPNST) and malignant glioma, including GBM **and to TNG462 for the treatment of soft tissue sarcoma** . Similarly, in **the** ~~Europe~~ **European Union** , the European Commission, upon the recommendation of the EMA' s Committee for Orphan Medicinal Products, grants orphan designation **in respect** ~~to promote the development~~ of ~~drugs~~ **products** that are intended for the diagnosis, prevention or treatment of life- threatening or chronically debilitating conditions affecting not more than five in 10, 000 persons in **the** ~~Europe~~ **European Union** and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation ~~is~~ **may be** granted for ~~drugs~~ **products** intended for the diagnosis, prevention, or treatment of a life- threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the ~~drug~~ **product** in **the** ~~Europe~~ **European Union** would be sufficient to justify the necessary investment in developing the ~~drug~~ **product** . In **the** ~~Europe~~ **European Union** , orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers. Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if **, at the end of the fifth year, it is established that** a product no longer meets the criteria for orphan ~~drug~~ designation ~~or if~~ **, including where it is shown that** the product is sufficiently profitable so that market exclusivity is no longer justified. Obtaining orphan drug exclusivity may not effectively protect a product candidate from competition because different products having different chemical compositions can be approved for the same condition and the same therapies can be approved for different conditions but used off- label. Even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a product nor gives the product any advantage in the regulatory review or approval process. While we may seek orphan drug designation for our **other** product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations. A breakthrough therapy designation and fast track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive regulatory approval in the United States. We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life- threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification and rescind the designation or decide that the time period for FDA review or approval will not be shortened. ~~We may also seek fast track designation for some of our product candidates and, in the case of TNG908 and TNG462, we have been granted fast track designation by the FDA.~~ If a drug is intended for the treatment of a serious or life- threatening condition and preclinical or clinical data demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this

designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program ~~. Fast track designation alone does not guarantee qualification for the FDA' s priority review procedures~~ . We may seek accelerated approval of our current or future product candidates using the FDA' s accelerated approval pathway. Accelerated approval by the FDA, even if granted for our current or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive regulatory approval. We may seek accelerated approval of our current or future product candidates, where applicable, using the FDA' s accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA requires that a sponsor of a drug receiving accelerated approval perform adequate and well- controlled post- marketing clinical trials. These confirmatory trials must be completed with due diligence. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post- approval confirmatory study or studies be under way prior to approval or within a specified time period after the date accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug' s predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post- approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre- approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of traditional FDA approval. The FDA, the EMA and other regulatory authorities may implement additional regulations or restrictions on the development and commercialization of our product candidates, and such changes can be difficult to predict. The FDA, the EMA and regulatory authorities in other countries have ~~each~~ expressed interest in further regulating biotechnology products. Agencies at both the federal and state level in the United States, as well as U. S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry **and the pharmaceutical industry, in particular** . Such **governmental** action **or actions** may delay or prevent commercialization of some or all of our product candidates. Adverse developments in clinical trials of products conducted **by us or** by others may cause the FDA or other oversight bodies to change the requirements for conducting clinical trials or for approval of any of our product candidates. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all. Inadequate funding for the FDA, the SEC and other U. S. government agencies or the EMA or comparable foreign regulatory authorities, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA, the EMA or comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and enact statutory, regulatory and policy changes. Average review times at the FDA or other regulatory authorities have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, ~~including~~ **and** those that fund research and development activities **that is required by third parties we enter into agreements with** , is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA, the EMA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, in prior years the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to

properly capitalize and continue our operations ~~. Separately, since March 2020 when foreign and domestic inspections were largely placed on hold due to the COVID- 19 pandemic, the FDA has been working to resume pre- pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre- approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID- 19 pandemic, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID- 19 pandemic~~ . If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA and other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Healthcare legislative reform measures may have a material adverse effect on our business and results of operations. Changes in regulations, statutes or the interpretation of existing regulations and statutes could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) changes to the method in which drug prices are determined for Medicare and Medicaid participants or other potential patients in the U. S. (or by which drug prices are determined in other countries and regions), (iii) additions or modifications to product labeling (if, and when, a product is approved for sale); (iv) the recall or discontinuation of our products (if any products are approved by applicable regulatory authorities); or (v) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. For additional information, see the section entitled " Business – Current and future healthcare reform legislation. " The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect: ? the demand for any of our product candidates, if approved; ? the ability to set a price that we believe is fair for any of our product candidates, if approved; ? our ability to generate revenues and achieve or maintain profitability; ? the level of taxes that we are required to pay; and ? the availability of capital. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements **. On August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022 (IRA), which, among other provisions, included several measures intended to lower the cost of prescription drugs and related healthcare reforms. This includes a provision that small molecule drugs can be chosen for price setting seven years after first approved by the FDA with the set price taking effect two years later, only nine years after the medicine was initially approved. This is far earlier than the time before small molecule medicines typically face generic competition. As a result, if we were to have one or more of our small molecule drugs approved by the FDA, under the IRA, we could be forced to sell our products at a lower price for CMS programs for several years earlier than would otherwise be the case. In addition, because this could result in lower future cash flows in those years, the future valuation of the company could be negatively impacted** . Further, reductions in reimbursement from Medicare and other government programs may also result in reductions in payments from private payers. In addition, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. 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 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. We expect that additional healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Additionally, we expect to experience pricing pressures in connection with the sale of any future approved product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes. The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those drugs and decrease our ability to generate revenue. The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third- party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by

governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. For more information regarding insurance coverage and reimbursement please see " Business – Government Regulation – Insurance Coverage and Reimbursement. " Government authorities and other third- party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third- party payor may depend upon a number of factors, including the third- party payor' s determination that use of a product is: ? a covered benefit under its health plan; ? safe, effective and medically necessary; ? appropriate for the specific patient; ? cost- effective; and ? neither experimental nor investigational. Even if we obtain coverage for our product candidates by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the U. S., the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. There is significant uncertainty related to the insurance coverage and reimbursement of newly- approved products. In the U. S., third- party payors, and governmental healthcare plans, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the U. S. for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third- party payors may require pre- approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our product candidates. Outside the U. S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe and other foreign jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates (if approved by regulators). Moreover, increasing efforts by governmental and third- party payors in the U. S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Our relationships with customers and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings. Although we do not currently have any products on the market, once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third- party payors play a primary role in the recommendation and prescription of any product candidates for which we may obtain regulatory approval. Our future arrangements with third- party payors, healthcare providers, and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain regulatory approval. See the section entitled " Business – Other healthcare laws. " Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including future sales of our product candidates (following regulatory approval of such therapy) by us or third- parties that we engage, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with appropriately licensed and permitted third parties for the disposal of these materials and wastes. We cannot, however, eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or

radioactive materials. Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post- market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements. Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion, monitoring, and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, establishment registration and listing, as well as continued compliance with cGMP and GCPs for any clinical trials that we conduct post- approval and pharmacovigilance reporting obligations. Manufacturers and other entities involved in the manufacture and distribution of approved drugs ~~or biologics~~ , and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies, and are subject to periodic announced and unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other regulatory requirements, including applicable product tracking and tracing requirements. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: ? restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls; ? manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation; ? revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings; ? imposition of a REMS which may include distribution or use restrictions; ? requirements to conduct additional post- market clinical trials to assess the safety of the product; ? clinical trial holds; ? fines, warning letters or other regulatory enforcement action; ? refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals; ? product seizure or detention, or refusal to permit the import or export of products; and ? injunctions or the imposition of civil or criminal penalties. The FDA' s and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. European data collection is governed by restrictive regulations governing the use, processing and cross- border transfer of personal information. We are conducting and plan to conduct additional clinical trials and enroll subjects in our current or future clinical trials in the U. S. and Europe, and therefore we will be subject to privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area (" EEA "), including personal health data, is subject to the EU General Data Protection Regulation, or GDPR and similarly, processing of personal data regarding individuals in the UK is subject to the UK General Data Protection Regulation and the UK Data Protection Act 2018, or UK GDPR and together with the EU GDPR, " GDPR ". The GDPR is wide- ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third- party processors. ~~While we have commenced~~ **The GDPR also imposes strict rules on** the ~~process~~ **transfer** of ~~implementing procedures~~ **personal data outside of the EEA and UK to countries that do not ensure an adequate level of protection, like the United States in certain circumstances unless a valid GDPR transfer mechanism (for example, the European Commission approved Standard Contractual Clauses (SCCs), and the UK International Data Transfer Agreement / Addendum (UK IDTA) has been put in place). Where relying on the SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. Any inability to transfer personal data from the EEA and UK to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. Failure** to comply with the GDPR, **and any supplemental EEA Member State or UK national data protection laws which may apply by virtue of the location of the individuals whose personal data we collect, may result in substantial penalties to which we could be subject in the event of any non- compliance, including potential fines of up to the greater of € 20 million (£ 17. 5 million under the UK GDPR) or up to 4 % of our total worldwide annual turnover for more serious offenses. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. While we have implemented procedures to comply with the GDPR, maintaining ongoing** compliance with these regulations will be a rigorous and time- intensive process that we expect will increase our cost of doing business and require us to **continue to** change certain of our business practices,

and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, many countries interpret the application of the provisions of the GDPR in different manner, making compliance in certain countries and across the EEA challenging **.The UK' s** data **protection regime,which** is ~~utilized,processed and stored~~ **independent from but aligned to the EU' s data protection regime** .Although the UK is regarded as a third country under the EU **' s** GDPR,the European Commission has issued a decision recognizing the UK as providing adequate protection under the EU GDPR (~~"~~Adequacy Decision ~~"~~) and,therefore,transfers of personal data originating in the EEA to the UK remain unrestricted.The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.The UK Government has also now introduced a Data Protection and Digital Information Bill (~~"~~UK Bill ~~"~~) into the UK legislative process ~~.The aim of the UK Bill is~~ to reform the UK' s data protection regime following Brexit.If passed,the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK ~~Adequacy~~ **adequacy** ~~Decision~~ **decision** from the ~~EU~~ **European** Commission ~~.This may lead to additional compliance costs and could increase our overall risk~~ .The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. ~~These and other~~ **This lack of clarity on** future ~~developments regarding~~ **UK laws and regulations and** ~~the~~ **their** ~~flow of data across borders~~ **interaction with EU laws and regulations** could ~~increase the~~ **add legal risk,complexity and** cost **to** ~~and complexity of delivering~~ our ~~services in some markets~~ **handling of personal data** and ~~may lead to governmental enforcement actions,litigation,fines,and penalties or~~ **our** ~~adverse publicity,which~~ **privacy and data security compliance programs and** could ~~adversely affect~~ **require us to implement different compliance measures for the UK and the EEA** . Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs. As we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U. S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non- U. S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. Risks Relating to Employee Matters and Managing Anticipated Growth Our future success depends on our ability to retain key executives and experienced scientists and to attract, retain and motivate qualified personnel. We are highly dependent on many of our key employees and members of our executive management team as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with certain of our executive officers, each of them may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and clinical trial and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. Recruiting and retaining qualified scientific, clinical, medical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees, including temporary loss due to illness, could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific, medical and clinical personnel from universities and research institutions. Failure to provide evidence of safety and efficacy of our product candidates in clinical trials, or delays experienced in such clinical trials, may make it more challenging to recruit and retain qualified scientific personnel. In particular, we have experienced a very competitive hiring environment in Boston and Cambridge, Massachusetts. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more

diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high- quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited. We may be unable to adequately protect our information **technology** systems from cyberattacks, **cyber intrusions or otherwise** which could result in ~~the~~ **damage to our information technology system and unauthorized** disclosure **or use** of confidential or proprietary information, including personal data ~~, damage our reputation, and subject us to significant financial and legal exposure~~ . We rely on information technology systems that we or our third- party providers operate to process, transmit and store electronic **health** information in our day- to- day operations. In connection with our ~~product discovery efforts, we collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers. In addition, in connection with our TNG908 and TNG462 Phase 1 / 2~~ clinical trials, we (and our third party processors assisting with the clinical ~~trial~~ **trials**) ~~will~~ **may** have access to **or** ~~, and may~~ store ~~,~~ clinical and health information of the patients participating in the ~~trial~~ **trials and such information may be accessed as result of a cyberattack, cyber intrusion or otherwise** . A **security breach, incident or compromise, whether through a** successful cyberattack **, cyber intrusion or otherwise,** could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, **computer viruses,** denial- of-service, social engineering ~~fraud~~ **tactics** or other means to threaten **the security, confidentiality, integrity and availability of our information technology systems and** data **. A** security **breach** , ~~confidentiality~~ **incident or compromise** , **whether through a** ~~integrity and availability. A~~ successful cyberattack **or otherwise,** could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including the compounds we are developing, our screening platform technology, financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we ~~devote resources~~ **have implemented various measures designed** to protect our information **technology** systems, ~~we realize that cyberattacks are a threat, and~~ there can be no assurance that our efforts will prevent ~~information~~ security breaches **, incidents or other compromises** that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches **, incidents** or **compromises could lead to** improper access to, use of, or disclosure of our **proprietary or confidential information (including** clinical data or patients' personal data **) and** could result in significant liability under **various data protection laws, including** state (e. g., state breach notification laws), federal (e. g., HIPAA, as amended by HITECH), and international ~~law~~ **laws** (e. g., the GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business. We rely on our third- party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches **of our systems** . If we or our third- party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third- party providers could have difficulty preventing, detecting and controlling such cyber- attacks and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, other expenses or lost revenue or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches **, incidents** or **compromises, or any** improper access to or disclosure of ~~such~~ **proprietary or confidential** information **,** could have ~~similarly~~ adverse consequences for ~~us~~ **our business and our reputation** . If we are unable to prevent or mitigate the impact of such security ~~or data privacy~~ breaches **, incidents, or other compromises** , we could be exposed to litigation and governmental investigations **and related fines and penalties. Several U. S. states have passed or enacted comprehensive privacy laws. California** , which **enacted** ~~could lead to a potential disruption to our business. By way of example,~~ the California Consumer Privacy Act, or CCPA **and its amendments** , **requires covered businesses to comply with specific** ~~which went into effect on January 1, 2020, creates individual~~ privacy ~~rights for~~ **and security obligations regarding their handling of personal information of** California consumers ~~and increases~~ **, such as providing** the ~~privacy and security obligations~~ **ability to opt- out** of ~~entities handling~~ certain ~~personal data~~ **sales or transfers** . The CCPA provides for civil penalties for violations, as well as a private right of action for **certain types of** data breaches ~~that is expected to increase data breach litigation~~ . ~~The~~ **A number of other U. S. states have passed or enacted comprehensive privacy legislation which are similar to the** CCPA ~~may increase our compliance costs and potential liability~~ , **but contain several key differences in their scope application** and **enforcement, which** ~~many~~ **may complicate our efforts and require additional resources and expenses in our effort to comply with them.** ~~similar~~ **Similar comprehensive consumer privacy** laws have been proposed ~~at the federal level and~~ in **numerous** other states. ~~Third parties that perform services on~~ **Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and / ~~our~~ or ~~behalf~~ changes** in **business practices** ~~connection with our research~~ and **policies. There are** ~~development efforts and other operations may~~ also **states** ~~hold proprietary or confidential information regarding our business on their information technology networks. The risks outlined above (and elsewhere in this risk factor) apply to any third- party service provider that holds our information, including the ability of unauthorized access to our confidential and proprietary information. Further, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information~~ that are ~~scheduled to take effect on January 1~~ **specifically regulating health information. For example** , ~~2023 (with certain provisions~~ **Washington state recently passed a health privacy law that will regulate the collection and** ~~having~~ **sharing of**

health information ~~retroactive effect to January 1~~ , ~~2022). Additionally~~ **and the law also has a private right of action** , ~~some observers~~ **which further increases the relevant compliance risk. Connecticut and Nevada** have **also passed similar** ~~noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U. S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level, for example, comprehensive privacy~~ laws **regulating consumer health data. In addition** ~~akin to the CCPA have recently been passed in Colorado~~ , ~~Utah, Virginia and Colorado, and, with bills being proposed in several~~ other ~~states, it is quite possible that other U. S. states will follow suit. New privacy and data security laws have been proposed in more than half of the states in the U. S. and in the U. S. Congress. Further, in addition to the proposals for comprehensive consumer privacy laws, many states are considering more limited privacy bills that focus on specific issues such as biometric data. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly. A number of states have adopted privacy laws and several~~ states have proposed ~~new~~ **and / or passed legislation that regulates the** privacy ~~laws, some~~ **and / or security** of ~~which are similar to the above discussed recently~~ **certain specific types of information. For example, a small number of states have** passed laws **that regulate biometric data specifically** . ~~Such proposed legislation~~ **These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U. S. Congress of a new comprehensive federal data privacy law to which we may likely become subject** , if enacted **. These laws demonstrate our vulnerability to** ~~, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and~~ the ~~availability of previously useful~~ **evolving regulatory environment related to personal** data **. As we expand our operations, these** and ~~could result in similar laws may increased~~ **increase our** compliance costs and **potential** ~~/ or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur~~ liability for noncompliance. To enable the transfer....., financial condition and results of operations . If we or third- party CMOs, CROs or other contractors or consultants fail to comply with U. S. and international data protection laws and regulations, ~~it~~ **we** could **face** ~~result in~~ government enforcement actions (which could include civil or criminal penalties) ~~,~~ **or** private litigation, ~~and / which would require additional investment of resources, limit or~~ **our ability to use personal data, and result in** adverse publicity ~~and~~ **which** could negatively affect our operating results and business. ~~Moreover, clinical trial subjects about whom we, our CRO operating our trials, or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information.~~ Claims that we or ~~such~~ **our** third-party **service providers** have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could ~~be expensive and time- consuming to defend and could~~ result in adverse publicity that could harm our business **, increase our costs and negatively affect our reputation. Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information, and personal data. Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. We may integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. In addition, our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third- party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. We also expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU' s Artificial Intelligence Act (AI Act) — the world' s first comprehensive AI law — is anticipated to enter into force in Spring 2024 and, with some exceptions, become effective 24 months thereafter. This legislation imposes significant obligations on providers and deployers of high risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. If we develop or use AI systems that are governed by the AI Act, it may necessitate ensuring higher standards of data quality, transparency, and human oversight, as well as adhering to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business** . We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. As of December 31, ~~2022~~ **2023** , we had ~~110~~ **140** full- time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly as we function as a public company and in the areas of product development, regulatory affairs and, if any of our product candidates receives regulatory approval, sales, medical affairs, marketing and distribution. To manage our anticipated future growth, we

must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the planned expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. Risks Related to Our Common Stock Our ~~executive officers, directors,~~ principal stockholders ~~and their affiliates~~ own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. Based on our common stock outstanding as of December 31, ~~2022~~ **2023** , **a limited number of shareholders** ~~our executive officers, directors and their affiliates and our principal stockholders beneficially held~~ **hold** ~~, in the aggregate~~ --- **greater than a majority** ~~, approximately 40 %~~ of our outstanding voting stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. These stockholders may have interests, with respect to their common stock, that are different from those of other investors and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by delaying, deferring or preventing a change of control of us, impeding a merger, consolidation, takeover or other business combination involving us or discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us. Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited. Under Sections 382 and 383 of the Internal Revenue Code, as amended, or the Code, if a corporation undergoes an " ownership change " (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity over a three- year period), the corporation' s ability to use its pre- change net operating loss carryforwards and certain other pre- change tax attributes to offset its post- change income may be limited. We have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. The Company has performed an analysis of ownership changes through December 31, 2021, and determined that on February 6, 2017 and August 17, 2020, ownership changes had occurred. Based on this analysis, the Company' s ability to use its pre- change tax attributes to offset federal and state taxable income are subject to annual limitations and a portion of the attributes generated prior to February 6, 2017, will expire unutilized, which could potentially result in an increased future tax liability. The Company has adjusted its deferred tax assets and valuation allowance balance for the affected tax attribute carryforwards to reflect the expiration of the attributes. Federal net operating loss carryforwards generated in taxable years beginning after December 31, 2017 will not be subject to expiration. However, any such net operating loss carryforwards may only offset 80 % of our annual taxable income in taxable years beginning after December 31, 2020. There is also a risk that due to regulatory changes, such as suspensions on the use of net operating loss carryforwards or other unforeseen reasons, our existing net operating loss carryforwards could expire or otherwise be unavailable to offset future income tax liabilities, including for state tax purposes. In future years, if and when a net deferred tax asset is recognized related to our net operating loss carryforwards, the changes in the carryforward / carryback periods as well as the new limitation on use of net operating loss carryforwards may significantly impact our valuation allowance assessments for net operating loss carryforwards. For these reasons, we may not be able to utilize some portion of our net operating loss carryforwards, none of which are currently reflected on our balance sheet, even if we attain profitability. Anti- takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Our certificate of incorporation and bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include: ? a board of directors divided into three classes serving staggered three- year terms, such that not all members of the board will be elected at one time; ? a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders; ? a requirement that special meetings of the stockholders may be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons; ? advance notice requirements for stockholder proposals and nominations for election to our board of directors; ? a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and then, in addition to any other vote required by law, only upon the approval of not less than 66 2 / 3 % of all outstanding shares of our capital stock then entitled to vote in the election of directors; ? supermajority voting requirements to amend our bylaws by stockholder action (unless our board recommends that our stockholders approve such amendment (s)) and to amend specific provisions of our certificate of incorporation; and ? the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock. These anti- takeover provisions and other provisions in our certificate of incorporation and bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then- current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or

cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline. Our bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us. Pursuant to our bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, or the DGCL, or our certificate of incorporation or bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim governed by the internal affairs doctrine. We refer to the foregoing provision as the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. We refer to such provision as the Federal Forum Provision. Our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U. S. federal securities laws and the rules and regulations thereunder. The Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. While the Delaware Supreme Court and courts in other states have upheld federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on us and / or our stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders. We are subject to certain U. S. and foreign anti-corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations. Among other matters, U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners and representatives from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We also expect our non- U. S. activities to increase in time. We have, and we expect we will continue to, engage third parties for clinical trials and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, representatives or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, imposition of a monitor, possible exclusion from participation in federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Because we do

not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock. Our stock price has been and is likely to continue to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock. The market price for our common stock may be influenced by many factors, including: ? the success **or failure** of competitive products or technologies; ? advancement of our preclinical programs ~~, such as our targeted oncology programs,~~ into clinical testing; ? results of clinical trials of our product candidates or those of our competitors; ? regulatory or legal developments in the United States and other countries; ? developments or disputes concerning patent applications, issued patents or other proprietary rights; ? the recruitment or departure of key personnel; ? the level of expenses related to any of our programs and product candidates or preclinical and clinical development programs; ? the results of our efforts to discover, develop, acquire or in- license additional product candidates or products; ? actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; ? variations in our financial results or those of companies that are perceived to be similar to us; ? changes in the structure of healthcare payment systems and third- party reimbursement decisions; ? market conditions in the pharmaceutical and biotechnology sectors; ? purchases or sales of our securities by our officers, directors or significant shareholders; ? limited trading volume; ? general economic, industry and market conditions; and ? the other factors described in this " Risk Factors " section. We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives. As a public company, and particularly after we are no longer an " emerging growth company, " we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes- Oxley Act and rules subsequently implemented by the SEC and The Nasdaq Global Market, or Nasdaq, have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time- consuming and costly. For example, these rules and regulations have made it more expensive for us to obtain director and officer liability insurance. Pursuant to Section 404 of the Sarbanes- Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well- conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not control these analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price target for our stock or publish inaccurate or unfavorable evaluations of our company or our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to publish reports covering our company regularly, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. In addition, if we are the subject of negative publicity, whether from an analyst, academic, industry group or the general or financial press, our stock price may decline. We may be subject to securities litigation, which is expensive and could divert management attention. The market price of our common stock has been and may continue to be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that

have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management' s attention from other business concerns, which could seriously harm our business. General Risk Factors Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, could adversely affect our business operations, financial condition and results of operations. Actual events involving limited liquidity, defaults, non- performance or other adverse developments that affect financial institutions or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, ~~on~~ **in** March ~~10,~~ 2023, Silicon Valley Bank (~~"~~ SVB ~~"~~) was closed by the California Department of Financial Protection and Innovation **and** ~~, which appointed the Federal Deposit Insurance Corporation (" FDIC ") as receiver. Similarly, on March 12, 2023,~~ Signature Bank and Silvergate Capital Corp. were each swept into receivership. ~~Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder.~~ We did hold certain funds in a deposit account with SVB, and while we now have access to those funds, we did not have access for a short time leading up to the events on March 10, 2023. ~~Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U. S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $ 25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.~~ Although we assess our banking relationships as we believe necessary or appropriate, our access to **funding** ~~our cash resources~~ -- **sources** ~~are~~ **in amounts** adequate to ~~fund~~ **finance** ~~our~~ -- **or capitalize our current and projected future business** operations **could be significantly impaired** ~~into at least 2025. But if the banks in which we hold our cash and cash equivalents were to experience bankruptcy or suspend operations, in such case, the amounts above the level insured~~ by **factors caused by** the **financial services industry** ~~FDIC may not be available to us immediately,~~ or ~~at all~~ **economy in general** . ~~The results of events or concerns that involve one or more of these~~ **These** factors could include ~~a variety of material and adverse impacts on~~ **, among others, events such as liquidity constraints** ~~our~~ -- **or** ~~current and projected business operations and our~~ **failures, the ability to perform obligations under various types of** financial ~~condition and results of operations. These could include~~ , **credit** ~~but may not be limited to, the following: • Delayed access to deposits~~ or **liquidity agreements or arrangements, disruptions or instability in** ~~other~~ -- **the** financial ~~assets~~ **services industry** or ~~the uninsured loss of deposits or other~~ financial **markets** ~~assets; or • Termination of cash management arrangements and / or delays in accessing or actual loss of funds subject to cash management arrangements. In addition~~ , ~~investor~~ **or** concerns ~~regarding~~ **or negative expectations about** the **prospects** ~~U. S. or~~ **for** ~~international~~ **companies in the** financial **services industry** ~~systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and / or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and / or projected business operations and financial condition and results of operations~~ . In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and / or projected business operations and results of operations and financial condition. Comprehensive tax reform legislation could adversely affect our business and financial condition. The tax regimes we are subject to or operate under are unsettled and may be subject to significant change. Changes in tax laws ~~(including in response to the COVID- 19 pandemic)~~ or tax rulings, or changes in interpretations of existing laws, could cause us to be subject to additional income- based taxes and non- income taxes (such as payroll, sales, use, value- added, digital tax, net worth, property, and goods and services taxes), which in turn could materially affect our financial position and results of operations. Additionally, new, changed, modified, or newly interpreted or applied tax laws could increase our potential future customers' and our compliance, operating and other costs, as well as the costs of our products, if approved. As we expand the scale of our business activities, any changes in the U. S. taxation of such activities may increase our effective tax rate and harm our business, financial condition, and results of operations. Complying with these tax laws is complex and the statutes and regulations can be subject to varying interpretation which can make compliance challenging. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the United States and other countries ~~are~~ **have** ~~experiencing~~ **experienced** increased inflation and interest rates ~~have~~ increased in response to this inflation **.** These conditions in the U. S. and global economy have caused significant volatility and uncertainty in U. S. and international markets. A severe or prolonged economic downturn, a marked increase in interest rates and inflation could result in a variety of risks to our business, including, weakened demand for our product candidates (if and when approved by regulatory authorities) and our ~~ability~~ **inability** to raise additional capital when needed on acceptable terms, if at all. In addition, our business may be

generally exposed to the impact of political or civil unrest or military action, including the current conflict between Russia and Ukraine (where a vendor that performs chemistry related work on our pre- clinical product candidates is located) and, while we do not otherwise have direct exposure to Ukraine, our business and results of operations may be impacted based upon the events taking place there. A weak or declining economy could also strain our suppliers and the global supply chain, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. An active trading market for our common stock may not be sustained, and you may not be able to resell your shares at the price you paid. Although our common stock is listed on The Nasdaq Global Market, an active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, investors may be unable to sell their shares.