Risk Factors Comparison 2024-03-21 to 2023-03-22 Form: 10-K

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

· We have never been profitable and may never achieve or sustain profitability. If we are unable to generate sufficient revenue from our operations to pay expenses or we are unable to obtain additional financing on commercially reasonable terms, our business, financial condition and results of operations may be materially and adversely affected. · We will require substantial additional funding to achieve our goals. Failure to obtain this necessary capital when needed on acceptable terms, or at all, may force us to delay, limit or terminate our product development efforts, other operations or commercialization efforts. · Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates. · ~~Our failure~~ **We may not continue** to meet the continued listing requirements of ~~The~~ **the** Nasdaq ~~Capital~~ **Stock** Market **(" Nasdaq "), which** could result in a ~~de- listing~~ **delisting** of our common **shares** ~~stock. Failure to regain compliance with Nasdaq listing rules could affect the market price of our Common Stock and liquidity and reduce our ability to raise capital~~ . · Our business is substantially dependent on the success of the DNase oncology platform. · We operate in an extremely competitive environment and there can be no assurances that competing technologies would not harm our business development. · We are an early- stage company in the business of developing pharmaceutical products including drug candidates and technologies. Given the uncertainty of such development, our business operations may never fully materialize and create value for investors. · If conflicts arise between us and our collaborators or strategic partners, these parties may act in their self- interest, which may limit our ability to implement our strategies. · We expect to rely on third parties to conduct, supervise and monitor our clinical studies, and if these third parties perform in an unsatisfactory manner, it may harm our business. · Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products. · We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans. · If we enter into one or more collaborations, we may be required to relinquish important rights to and control over the development of our drug candidates or otherwise be subject to unfavorable terms. ~~iv.~~ · We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our pharmaceutical products. **iv** · We may encounter substantial delays in commencement, enrollment or completion of our clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing our current and future drug candidates on a timely basis, if at all. · If we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a drug candidate, or the approval may be for a more narrow indication than we expect. · If we obtain regulatory approval for a drug candidate, our drug candidate will remain subject to regulatory scrutiny. · The commercial success of any current or future pharmaceutical products will depend upon the degree of market acceptance by physicians, patients, third- party payors and others in the medical community. · The commercial potential of a pharmaceutical candidate in development is difficult to predict. If the market size for a new drug candidate or technology is significantly smaller than we anticipate, it could significantly and negatively impact our revenue, results of operations and financial condition. · Failure to obtain or maintain adequate coverage and reimbursement for our drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. · We may use our financial and human resources to pursue a particular research program or drug candidate and fail to capitalize on programs or drug candidates that may be more profitable or for which there is a greater likelihood of success. · We may not be successful in our efforts to identify or discover additional pharmaceutical products. · The market opportunities for our drug candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small. · We have no manufacturing, sales, marketing or distribution capabilities, and we may have to invest a significant amount of resources to develop these capabilities. · Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. · If we fail to adequately protect or enforce our intellectual property rights, we may be unable to operate effectively. · Issued patents covering our drug candidates could be found invalid or unenforceable if challenged in court. · We may not be able to protect our intellectual property rights throughout the world. · If we infringe on the intellectual property rights of others, our business and profitability may be adversely affected. ~~v.~~ · If we fail to comply with our obligations in the agreements under which we 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 be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. **v** · We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. · Our inability to protect our confidential information and trade secrets would harm our business and competitive position. · Our future success depends on our ability to retain principal members of our executive team, consultants and advisors and to attract, retain and motivate qualified personnel. · We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations. · We are a party to collaboration agreements and other significant agreements which contain complex commercial terms that could result in disputes, litigation or indemnification liability that could adversely affect our business, results of operations and financial condition. · The market price of our securities may be highly volatile, and you may not be able to sell our securities. · **Actions of activist shareholders could cause us to incur substantial costs, divert management' s attention and resources, and have an adverse effect on our business.** · Our preferred ~~stock has~~ **stockholders**

have rights, preferences and privileges that are not held by, and are preferential to, the rights of our common stockholders, which could result in the interests of ~~the holders of~~ our preferred ~~stock~~ **stockholders** differing from those of our common stockholders. vi PART I ITEM 1 – BUSINESS Overview We are a biopharmaceutical company focused on advancing innovative immune- oncology technologies addressing hard to treat cancers. Our proprietary DNase platform is designed to improve outcomes of existing treatments, including immunotherapies, by targeting NETs, which have been implicated in cancer progression and resistance to cancer treatments. ~~We licensed the DNase oncology platform in April 2022 and we have directed our efforts and resources on the development of this newly acquired technology.~~ The DNase platform is designed to target NETs, which are weblike structures composed of extracellular chromatin coated with histones and other proteins. NETs are expelled by activated neutrophils, in response to microbial or pro- inflammatory challenges. However, excessive production or reduced clearance of NETs can lead to aggravated inflammatory **, hypercoagulability** and autoimmune pathologies, as well as creation of pro- tumorigenic niches in the case of cancer growth and metastasis. We ~~plan to~~ **are focused on** ~~advance~~ **advancing the development of our DNase platform** toward a first- in- human, multicenter, dose escalation and dose- expansion study of IV rhDNase I in subjects with locally advanced or metastatic solid tumors. Our systemic DNase program is initially targeting multi- billion- dollar indications including pancreatic **cancer (which includes pancreatic ductal adenocarcinoma (“ PDAC ”)), colorectal** carcinoma **(“ CRC ”) and other gastrointestinal cancers** . ~~Pancreatic~~ **These are all** cancer **indications with significant unmet need, and with opportunities for substantial improvement of the currently available therapeutic options. PDAC** has a low rate of early diagnosis, a high mortality rate and a poor five- year survival prognosis. Symptoms are usually non- specific and as a result, **PDAC** ~~pancreatic cancer~~ is often not diagnosed until it reaches an advanced stage. Once the disease has metastasized, or spread to other organs, it becomes especially hard to treat. Each year, about 185, 000 individuals globally are diagnosed with this condition; and in 2021, the Surveillance, Epidemiology and End Results program, or SEER, of the National Cancer Institute estimated that in the United States there would be approximately 60, 000 individuals diagnosed with pancreatic cancer. The overall five- year survival rate among pancreatic cancer patients is 7- 8 %, which constitutes the highest mortality rate among solid tumor malignancies; among those diagnosed with metastatic disease, the overall five- year survival rate is only 3 %. Recent developments that have improved the survival in many cancer types have not been effective for pancreatic cancer patients, highlighting the **urgent** need for the development of ~~new~~ **newer , more effective** therapeutic options. ~~Furthermore~~ **For those few patients that present with earlier stage PDAC** , **surgical resection followed by chemotherapy is possible, but for the majority of PDAC patients which present at diagnosis with advanced disease, chemotherapy is the only option, and has only very limited benefit.** ~~second~~ **Second** - line patients that were diagnosed already with metastatic disease have ~~very~~ **even** ~~few~~ **fewer** therapeutic options. The only approved regimen for second- line patients is Onivyde ® in combination with 5FU and LV. For these Stage IV at diagnosis patients reaching second- line therapy, median overall survival is only 4. 7 months (Macarulla et al, Pancreas 2020). **CRC is the second most common cause of cancer death in the United States after lung cancer. CRC is the third most commonly diagnosed cancer in males and the second in females, globally, according to the World Health Organization GLOBOCAN database. In the United States, CRC is the second most common cause of cancer death after lung cancer. According to data from the NCI’ s Surveillance, Epidemiology, and End Results (“ SEER) Program, it is estimated that in 2023 approximately 153, 000 individuals in the U. S. will be diagnosed with colon cancer, and an estimated 53, 000 will die of the disease. CRC is in decline in older patients (> 65 years) but that is offset by a steady increase in CRC diagnoses and deaths in individuals younger than 55 years of age. Despite continued overall declines, CRC is rapidly shifting to diagnosis at a younger age, at a more advanced stage, and in the left colon / rectum. If CRC is diagnosed at a localized stage, the 5- year survival rate is 91 %. However, if the cancer has spread to surrounding tissues or organs and / or the regional lymph nodes, the 5- year relative survival rate is 72 %. There are numerous treatment options for earlier stage CRC patients, but as they progress to advanced and metastatic disease (“ mCRC ”), those options become limited. Approximately 22 % of CRC cases have metastasis at presentation, and 19 % will develop metastasis after primary tumor removal. Unfortunately, if CRC has spread to distant parts of the body, the 5- year relative survival rate is 13 %. 1 All major guidelines recommend patients with mCRC undergo testing of DNA for high DNA microsatellite instability (MSI- H), a mutation found in approximately 10 % of all CRC, and up to 5 % of mCRC. CRC patients that are MSI- H / MMRd (or “ mismatch repair deficient ”) are candidates for immunotherapy using immune checkpoint inhibitors (“ ICIs ”); at present, there are three ICIs approved for MSI- H / MMRd CRC – Keytruda, Opdivo (anti- PD- 1 antibodies) and Yervoy (anti- CTLA- 4 antibody). While the ICI response rates in this small subset of CRC are encouraging at around 50 %, a significant number of patients are resistant, or become refractory to ICI therapy. However, the vast majority of mCRC patients (> 90 %) are microsatellite stable (“ MSS ”) and mismatch repair proficient (“ MMRp ”), where ICIs have not been shown to provide benefit. The lack of ICI response in this subset is due to poor immunogenicity and immunosuppression. Again, this highlights the urgent need for the development of newer, more effective therapeutic options.** A substantial amount of scientific literature has implicated NETs in the context of cancer pathogenesis and resistance to cancer therapies (including chemo, radio, and immunotherapies such as checkpoint inhibitors and cell therapies). In published reports, elevated levels of NETs have been a biomarker associated with poor prognosis in patients with a variety of **cancers and in particular, in gastrointestinal** cancers. In addition, resistance to existing therapeutic agents can involve the release of immunosuppressive signaling factors from NETs, or physical barriers created by NETs, which can impede the infiltration, activity, and survival of cytotoxic T cells in the tumor microenvironment. Published pre- clinical models have demonstrated the effectiveness of systemically administered DNase, alone or in combination with other agents, for the elimination of NETs and prevention of tumor growth and metastasis. We are currently focused on advancing our systemic DNase program into the clinic as an adjunctive therapy for pancreatic carcinoma and locally advanced or metastatic solid tumors **, including CRC** . Adoptive transfer of **Chimeric Antigen Receptor (“** CAR **”)** T cells has emerged as one of the most promising advances in cancer

immunotherapy. To successfully treat solid tumors, CAR T cells must be able to infiltrate, persist, and maintain anti- tumor function in a hostile tumor microenvironment that is itself adept at immunosuppression and conducive to tumor cell survival. Recent approaches to CAR T design include " armored " CAR- T cells, so named because they can express additional factors to resist immunosuppression or degrade physical components of the tumor' s extracellular matrix, including NETs. We intend to conduct pre- clinical research with the goal of demonstrating that armoring CAR T cells to secrete DNase can support depth and durability of response against solid tumor indications. Engineered CAR T cells, designed to recognize cancer- associated antigens, are capable of sustained and selective killing of tumor cells, with substantial reduction of tumor burden. CAR T therapies have exhibited remarkable clinical success against hematological malignancies but thus far have failed to demonstrate success in the context of solid tumors. Published evidence suggests that in addition to immunosuppressive factors, mechanical barriers formed by NETs can impede T- cell penetration and occlude T- cell contact with tumor cells. ~~1~~ **The conduct of several CAR T in vivo models has been a primary focus of our Scripps collaboration.** Our collaboration with Belgian Volition SARL Limited (" Volition ") is an early exploratory program to evaluate the potential combination of Volition' s Nu. Q ® technology and Xenetic' s DNase- Armored CAR T platform to develop proprietary adoptive cell therapies potentially targeting multiple types of solid cancers for which current CAR T cell therapies have shown limited or no effect. Under the terms of the collaboration agreement, Volition will fund a research program and the two parties will share proceeds from commercialization or licensing of any products arising from the collaboration. Epigenetically modified nucleosomes are present on tumor cell surfaces and within the tumor microenvironment of multiple types of solid cancers, and thus these nucleosomes may represent generalizable tumor antigens that are not limited to a single cancer type. Volition' s Nu. Q ® technology can specifically recognize and target epigenetically modified nucleosomes, while our DNase- Armored CAR T platform is designed to enhance the function of CAR T cells within solid tumor microenvironments. ~~XCART is our personalized CAR T platform technology engineered to target patient- specific tumor neoantigens, with a demonstrated proof of mechanism in B- cell Lymphomas. The XCART technology platform was designed to utilize an established screening technique to identify polypeptide domains that selectively bind to the unique B- cell receptor (" BCR ") on the surface of an individual lymphoma patient' s malignant B- cell clones. This BCR- selective targeting domain is engineered into the antigen- binding domain of a CAR, creating the possibility of a CAR T treatment that should only recognize a given patient' s malignant B- cell clones. We believe our personalized CAR T therapies have the potential to offer cancer patients substantial benefits over the existing standard of care and currently approved CAR T therapies. We have suspended development of the XCART platform as we prioritized the DNase platform and intend to focus our resources on development of the DNase programs.~~ Additionally, we have partnered with biotechnology and pharmaceutical companies to develop our proprietary drug delivery platform, PolyXen, and receive royalty payments under an exclusive license arrangement in the field of blood coagulation disorders. PolyXen is an enabling platform technology for protein and peptide drug delivery. It uses the biological polymer polysialic acid (" PSA ") to prolong the drug' s half- life and potentially improve the stability of therapeutic peptides and proteins. Both the site of attachment and the length of the PSA chain can influence the properties of the therapeutic by changing the apparent hydrodynamic radius of the molecule, which in turn, can enhance a number of the biological characteristics of the therapeutic. It can also be used for small molecule drugs. **2** We incorporate our patented and proprietary technologies into drug candidates currently under development with biotechnology and pharmaceutical industry collaborators to create what we believe will be the next- generation biologic drugs with improved pharmacological properties over existing therapeutics. Our drug candidates have resulted from our research activities or that of our collaborators and are in the development stage. As a result, we continue to commit a significant amount of our resources to our research and development activities and anticipate continuing to do so for the near future. To date, none of our drug candidates have received regulatory marketing authorization or approval in the U. S. by the Food and Drug Administration (" FDA ") nor in any other countries or territories by any applicable agencies. **As noted above, we are receiving ongoing royalties pursuant to a license of our PolyXen technology to an industry partner.** Although we hold a broad patent portfolio, the focus of our internal efforts in ~~2022~~ **2023** was on the licensing and advancement of our DNase platform ~~and on the development of our XCART platform technology~~. We were incorporated under the laws of the State of Nevada in August 2011. We, directly or indirectly, through our wholly- owned subsidiaries, Hesperix S. A. (" Hesperix ") and Xenetic Biosciences (U. K.) Limited (" Xenetic U. K. "), and the wholly- owned subsidiaries of Xenetic UK, Lipoxen Technologies Limited (" Lipoxen "), Xenetic Bioscience, Incorporated and SymbioTec, GmbH (" SymbioTec "), own various U. S. federal trademark registrations and applications, along with unregistered trademarks and service marks, including but not limited to XCART, OncoHist, PolyXen, ErepoXen and ImuXen. Our Strategy ~~In April 2022 we licensed the DNase platform. The DNase platform is designed to improve outcomes of existing treatments, including immunotherapies, by targeting NETs (see " Overview " and " Our Technology and Drug Candidates " for a description of the technology).~~ Our primary **focus is** ~~efforts are now~~ aimed at advancing the systemic DNase program into the clinic as an adjunctive therapy for pancreatic cancer and other locally advanced or metastatic solid tumors **, including CRC** . Our goal is to provide solutions in the treatment of solid tumors by improving response and overcoming resistance to checkpoint inhibitors, chemotherapy, and other standard of care treatments. We also intend to pursue industry collaborations and potential licenses to develop DNase for other uses and indications. ~~2~~ We intend to pursue orphan drug designations and accelerated approval pathways for relevant oncology indications as appropriate in both the U. S. and Europe. If our orphan oncology drug candidates are granted orphan drug designation, then we may benefit from certain key advantages of orphan status including certain market exclusivities. We intend to advance development of our DNase platform primarily through the use of contract manufacturing ~~and~~ **,** contract research organizations (" CROs ") **and academic institutions** in order to efficiently manage our resources. Continuous pipeline growth and advancement of out- licensed drug candidates is dependent, in part, on our ability to raise sufficient capital and to advance our existing co- development collaborations and strategic arrangements as well as enter into new such arrangements. Business Developments ~~Exclusive Sublicense Agreement On April 26, 2022, we entered into an Exclusive Sublicense Agreement (the " Sublicense Agreement ")~~

~~with CLS pursuant to which we received an exclusive license, under certain patent rights and know- how owned or controlled by CLS, to develop and commercialize pharmaceutical products and methods incorporating DNase enzyme for use in treatment of cancer (the " Sublicensed Products "). Under the terms of the Sublicense Agreement, we will have sole responsibility for, and shall use commercially reasonable efforts to, among other things, research, develop and obtain marketing approval for the Sublicensed Products in the U. S. and certain European markets, and to commercialize such Sublicensed Products in the relevant market once marketing approval is obtained. In consideration for the license and other rights granted to us under the Sublicense Agreement, we issued to CLS 375, 000 shares of our common stock (the " Sublicense Agreement Shares "), of which 250, 000 Sublicense Agreement Shares were issued directly to OPKO Health, Inc. (" OPKO ") in lieu of transfer indirectly from CLS to EirGen Pharma Ltd. (" EirGen "), a wholly owned subsidiary of OPKO, in satisfaction of certain third- party contractual obligations between CLS and EirGen. Additionally, we are obligated to pay to CLS up to $ 13, 000, 000 in cash in potential milestone payments for the achievement of certain clinical and regulatory milestones, as well as issue an additional 950, 000 shares of our common stock to CLS based on the achievement of certain regulatory milestones. In addition, we are obligated to pay tiered royalties ranging from the mid- single to low- double digits on net sales of licensed products falling within the scope of the license during the Royalty Term (as defined in the Sublicense Agreement), as well as pay a percentage share in the low- to- mid teens of certain consideration received by us from any sublicensees. Exclusive License Agreement On April 26, 2022, we entered into an Exclusive License Agreement (the " License Agreement ") with CLS, pursuant to which we received an exclusive license under certain patent rights and know- how owned or controlled by CLS to develop and commercialize pharmaceutical products and methods incorporating DNase in conjunction with CAR- T therapies (the " Licensed Products "). Under the terms of the License Agreement, we will have sole responsibility for, and shall use commercially reasonable efforts to, among other things, research, develop and obtain marketing approval for the Licensed Products in the U. S. and certain European markets, and to commercialize such Licensed Products in the relevant market once marketing approval is obtained. In consideration for the license and other rights granted to us under the License Agreement, we paid CLS a one- time fee of $ 500, 000 in cash, issued to CLS 500, 000 shares of our common stock, and are obligated to pay up to $ 13, 000, 000 in cash in potential milestone payments for the achievement of certain clinical and regulatory milestones for each Licensed Product. In addition, we are obligated to pay tiered royalties ranging from the mid- single to low- double digits on net sales of licensed products falling within the scope of the license during the Royalty Term (as defined in the License Agreement), as well as pay a percentage share in the mid- teens to low double digits of certain consideration we receive from any sublicensees. 3 Patent Assignment and~~ Volition Collaboration ~~On October 4, 2022, we completed a patent assignment related to our collaboration with Volition and CLS. In connection with the patent assignment, we entered into a Subscription Agreement with CLS Therapeutics, LLC, a Delaware limited liability company (" CLS LLC "), on October 12, 2022, pursuant to which we agreed to issue to CLS LLC, and CLS LLC agreed to subscribe for, 850, 000 shares of our common stock as consideration for the assignment by CLS and its affiliates to us of certain patent rights owned by CLS and its affiliates.~~ On August 2, 2022, we announced a research and development collaboration with Volition to develop NETs- targeted adoptive cell therapies for the treatment of cancer. The collaboration is an early exploratory program to evaluate the potential combination of Volition' s Nu. Q ® technology Test and ~~our~~ **the Company' s** DNase- Armored CAR T platform to develop proprietary adoptive cell therapies potentially targeting multiple types of solid cancers. Under the terms of the collaboration agreement, Volition will fund a research program and the two parties will share proceeds from commercialization or licensing of any products arising from the collaboration. ~~Catalent~~ On ~~June 30~~ **July 10** , ~~2022~~ **2023** , we entered into ~~a~~ **the first Collaborator** Statement of Work **as part of this collaboration with Volition. 3 Scripps Research Institute** (~~the~~ " ~~SOW~~ **Scripps Research** ") ~~with Catalent Pharma Solutions LLC (" Catalent ") to outline the general scope of work, timeline, and pricing pursuant to which Catalent will provide certain services to us to perform cGMP manufacturing of our recombinant protein, Human DNase I. Scripps Research~~ On March 17, 2023, ~~we~~ **the Company and Scripps Research,** entered into a Research Funding and Option Agreement (the " Agreement ") **,** ~~with Scripps Research~~ pursuant to which we ~~have~~ agreed to provide Scripps Research an aggregate of up to $ 938, 000 to fund research relating to advancing the pre- clinical development of **our** ~~the Company' s~~ DNase oncology platform technology. The research funding is payable by us to Scripps Research on a monthly basis in accordance with a negotiated budget, which provides for an initial payment of approximately $ 78, 000 on the date of the Agreement and subsequent monthly payments of approximately $ 78, 000 over a 12- month period. Under the Agreement, we have the option to acquire a worldwide exclusive license to Scripps Research' s rights in the Technology or Patent Rights (as defined in the Agreement), as well as a non- exclusive, royalty- free, non- transferrable license to make and use TSRI Technology (as defined in the Agreement) solely for our internal research purposes during the performance of the research program contemplated by the Agreement. Unless earlier terminated, the term of the Agreement continues from the date of the Agreement for fifteen (15) months. The Agreement may be terminated by us with 30 days advance written notice to Scripps Research beginning six (6) months after the Effective Date (as defined in the Agreement) or by Scripps Research if we fail to make timely payments due under the Agreement, subject to 30 days' written notice to cure such nonpayment. The Agreement may further be terminated by either party in the event of the other party' s uncured failure to perform any obligations under the Agreement or the bankruptcy of the other party. **University of Virginia (" UVA ") On December 21, 2023, we entered into a Research Funding and Material Transfer Agreement, as amended, with UVA (the " UVA Agreement ") to advance the development of our systemic DNase program. Under the terms of the UVA Agreement, in addition to advancing our existing intellectual property, we have an option to acquire an exclusive license to any new intellectual property arising from the DNase research program. Allan Tsung, MD, a member of the Company' s Scientific Advisory Board and Chair of the Department of Surgery at the UVA School of Medicine, will oversee the research conducted under the UVA Agreement. As a surgical oncologist and scientist, Dr. Tsung is internationally recognized for leading substantial research on the role of NETs in tumor growth, metastasis, and resistance to existing cancer therapies. Our Technology and Drug Candidates** The Technologies We incorporate our

patented and proprietary technologies into a number of drug candidates which are currently under development internally or with our biotechnology and pharmaceutical collaborators, with the goal of creating what we believe will be the next generation of biologic drugs and therapeutics. While we primarily focus on researching and developing oncology drugs, we also have ownership and other economic interests in drugs being developed by our collaborators to treat other conditions. During the year ended December 31, ~~2022~~ **2023** , the focus of our internal development efforts was on the ~~licensing and~~ advancement of our DNase oncology platform ~~and the development of our XCART technology~~ . We have not been actively pursuing development efforts for **XCART or** PolyXen or any of our other technologies. ~~4~~ DNase The DNase platform is designed to target NETs, which are weblike structures composed of extracellular chromatin coated with histones and other proteins. NETs are expelled by activated neutrophils, in response to microbial or pro- inflammatory challenges. However, excessive production or reduced clearance of NETs can lead to aggravated inflammatory and autoimmune pathologies, as well as creation of pro- tumorigenic niches in the case of cancer growth and metastasis. Program Highlights: · Exclusive license and sublicense agreements with CLS **Therapeutics Ltd. (" CLS ")** to develop its interventional DNase platform, which is aimed at improving outcomes of existing treatments, including immunotherapies; · **Multiple value** ~~Advancing toward first~~ ~~in~~ **driving milestones expected over the next 12** - **24 months** ~~human study start targeted for 2024- 2025~~ ; · Systemic DNase program initially targeting multi- billion- dollar indications including pancreatic carcinoma and other locally advanced or metastatic solid tumors; and · DNase- armored CAR T program in early pre- clinical development. **4** XCART The **Chimeric Antigen Receptor (" CAR ") T cell (" XCART ")** technology platform was designed by its originators to utilize an established screening technique to identify peptide ligands that bind specifically to the unique BCR on the surface of an individual patient' s malignant tumor cells. The peptide is then inserted into the antigen- binding domain of a CAR T cell, and a subsequent transduction / transfection process is used to engineer the patient' s T cells into a CAR T format which redirects the patient' s T cells to attack the tumor. Essentially, the XCART screening platform is the inverse of a typical CAR T screening protocol wherein libraries of highly specific antibody domains are screened against a given target. In the case of XCART screening, the target is itself an antibody domain, and hence highly specific by its nature. The XCART technology creates the possibility of personalized treatment of lymphomas utilizing a CAR with an antigen- binding domain that should only recognize, and only be recognized by, the unique BCR of a particular patient' s B- cell lymphoma. An expected result for XCART is limited off- tumor toxicities, such as B- cell aplasia. We have suspended further development of XCART at this time, as we focus our efforts and resources on our DNase technology platform. PolyXen An enabling biological platform technology designed to extend the circulation time of drug molecules in the human body by chemically attaching PSA, to the drug molecule by a process termed polysialylation, thereby creating potentially superior next generation therapeutic candidates. PSA, a biopolymer, comprising a chain of sialic acid molecules, is a natural constituent of the human body, although we obtain our PSA from a bacterial source. Research, Outside Services and Collaborations Through partner efforts, we are developing our pipeline of next- generation bio- therapeutics and novel oncology drugs based on our DNase ~~, XCART~~ and PolyXen proprietary technologies. In order to do this while efficiently managing our overhead, we rely on the services of contract manufacturers, CROs and our strategic collaborations. We currently do not have in- house research facilities to pursue these initiatives. Accordingly, continuous pipeline growth and advancement of our technologies and drug candidates is dependent on several important collaborations and strategic arrangements, including our arrangements with: · Catalent **Pharma Solutions LLC (" Catalent ")** , a global leader in enabling biopharma, cell, gene and consumer health partners to optimize development, launch, and supply of better patient treatments across multiple modalities; · **PJSC** Pharmsynthez **(" Pharmsynthez ")** , including its wholly- owned subsidiary SynBio LLC (" SynBio "), a beneficial owner of approximately ~~2~~ **3** . ~~9~~ **4** % of our common stock; ~~and~~ · ~~The~~ Scripps Research ~~Institute (" Scripps Research ")~~ , one of the world' s largest, private non- profit research organizations **; and · The University of Virginia, a non- profit, educational, research and healthcare institution** . Accordingly, in addition to pursuing our development of the DNase technology, we also have significant interests in drug candidates being developed by our collaborators to treat other conditions. We may collect some combination of milestone payments and royalties pursuant to these collaborations to the extent that these drugs are successfully developed and marketed. However, other than royalty payments under a sublicense with Takeda **Pharmaceutical Co. Ltd. (together with its wholly- owned subsidiaries, " Takeda ")** and potential royalty payments under our collaboration agreement with Pharmsynthez, we do not anticipate any milestone or royalty payments in the near term, if at all. For further detail, please read the section titled " Significant Collaborations and Strategic Arrangements " below. 5 Our Drug Candidate Pipeline Our product pipeline contains drug candidates under development internally and with our biotechnology and pharmaceutical collaborators. The following table summarizes key information regarding our current drug candidates: ErepoXen, or polysialylated erythropoietin (" PSA- EPO "), uses our PolyXen platform technology for the treatment of anemia in chronic kidney disease (" CKD ") patients. It is designed to reduce the dosing frequency by extending the circulating half- life of the therapeutic in the body. We are not pursuing clinical development of ErepoXen but continue to entertain out- license opportunities for the drug candidate in our licensed territories. We have collaboration agreements with Pharmsynthez and Serum Institute to develop and launch ErepoXen in limited markets pursuant to which we will collect royalties if they are successful in these efforts. ~~6~~ Pharmsynthez received regulatory approval to commence a Phase II (b) / III human clinical trial of ErepoXen (also known as Epolong) in Russia with patient recruitment completed in 2020. In December 2020, Pharmsynthez reported positive data from this clinical trial and, in February 2021, reported in a press release that it had started the registration phase of Epolong by filing a registration dossier to obtain approval in Russia. Pharmsynthez had reported in its press release that it expected that the Russian stage of registration activities would be completed in 2021 and that it would be able to start production of the product as early as the first quarter of 2022. **In the first quarter of 2023,** Pharmsynthez ~~has~~ informed us that it had received a response letter indicating certain deficiencies in the dossier and **continues to develop a gap mitigation strategy with the** ~~intends~~ **intent** ~~to refile~~ **of refiling** the registration upon correction. **6** Serum Institute conducted Phase I and Phase II clinical trials of ErepoXen in ninety- five human subjects. These safety trials, which had no significant drug- related adverse

events, provided us with the data to commence a Phase II, repeat dosing, International Conference on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use compliant clinical trial for ErepoXen in Australia, New Zealand and South Africa for CKD patients not on dialysis. We completed three cohorts of this study and then terminated the study. In addition, Serum Institute finished Phase I / II clinical trials in India of ErepoXen for in- center- dialysis patients. Serum Institute may seek to leverage Pharmsynthez' s trial data and potential Russian marketing authorization to request a waiver for a Phase III clinical trial in India, subject to local regulatory authority approval. Pipeline Expansion Opportunities Operating under licenses from us within their home markets, our collaborators can potentially generate preclinical and clinical data related to our technologies across a wide spectrum of therapeutic areas. Under these agreements, we retain all rights for major markets and co-own the clinical data. We therefore have the opportunity to utilize the data in our decision- making process regarding development and commercialization in major markets. In October 2017, we granted to Takeda the right to grant a non- exclusive sublicense to certain patents related to **our** ~~the Company' s~~ PolyXen technology that were previously exclusively licensed to Takeda in connection with products related to the treatment of blood and bleeding disorders. ~~Pursuant to the agreement, Takeda (i) paid us a one- time payment of seven million five hundred thousand dollars ($ 7, 500, 000) in November 2017 and (ii) agreed to pay us single digit royalty payments based upon net sales of the covered products throughout the term.~~ Royalty payments ~~on net sales commenced in late 2019. Royalty payments~~ of approximately $ ~~1~~ **2** . ~~7~~ **5** million and $ 1. ~~2~~ **7** million were recorded as revenue by **us** ~~the Company~~ during the years ended December 31, **2023 and** 2022 ~~and 2021~~, respectively, and are based on single digit royalties on net sales of certain covered products. On ~~June 30~~ **April 26** , 2022, we entered into **an Exclusive Sublicense Agreement (the " Sublicense Agreement ") with CLS pursuant to which we received an exclusive license under certain patent rights and know- how owned or controlled by CLS, to develop and commercialize certain pharmaceutical products and methods incorporating DNase enzyme for use in the treatment of cancer (the " Sublicensed Products "). Under the terms of the Sublicense Agreement, we will have sole responsibility to, and shall use commercially reasonable efforts to, among other things, research, develop and obtain marketing approval for the Sublicensed Products in the U. S. and certain European markets, and to commercialize such Sublicensed Products in the relevant market once marketing approval is obtained. Concurrent with the Sublicense Agreement, we entered into an Exclusive License Agreement (the " License Agreement ") with CLS, pursuant to which we received an exclusive license under certain patent rights and know- how owned or controlled by CLS to develop and commercialize certain pharmaceutical products and methods incorporating DNase in conjunction with CAR T therapies (the " Licensed Products "). Under the terms of the License Agreement, we will have sole responsibility to, and shall use commercially reasonable efforts to, among other things, research, develop and obtain marketing approval for the Licensed Products in the U. S. and certain European markets, and to commercialize such Licensed Products in the relevant market once marketing approval is obtained. On August 2, 2022, we announced** a **research and development collaboration with Volition to develop NETs-targeted adoptive cell therapies for the treatment of cancer and on July 10, 2023 we entered into the first Collaborator Statement of Work with Volition as part of this collaboration. For more information regarding such collaboration with Volition, refer to the section titled " Business Developments " above. 7 On June 30, 2022, we entered into a Statement of Work (the "** SOW **")** with Catalent to outline the general scope of work, timeline, and pricing pursuant to which Catalent will provide certain services to us to perform **current Good Manufacturing Practices ("** cGMP **")** manufacturing of our recombinant protein, Human DNase I. The parties agreed to enter into a Master Services Agreement (" MSA ") that will contain terms and conditions to govern the project contemplated by the SOW and that will supersede the addendum to the SOW containing Catalent ~~'~~ **'** s standard terms and conditions. In addition, in the event of any conflict between the project- specific terms and conditions set forth in the SOW and the MSA, the MSA terms and conditions shall govern. The estimated total cost of the project contemplated by the SOW is expected to be up to approximately $ 5 million (exclusive of certain fees and potential alternatives) for the manufacturing services over the course of the term of the project with each phase of the project invoiced separately in connection with the commencement of such phase. **On March 17** ~~Unless earlier amended or terminated , the manufacturing services contemplated by the SOW are currently targeted to be completed by the first half of 2024~~ **2023 ,** ~~. The SOW is terminable by~~ the Company ~~at any time with 30 days' prior written notice to Catalent. The SOW also contains customary provisions related to, among other things, confidentiality, warranties, intellectual property~~ and **Scripps Research** ~~indemnification. 7 On May 15, 2020, we~~ entered into **the** ~~a Research Funding and Option~~ Agreement ~~with Scripps Research (the " Scripps Agreement ")~~, pursuant to which we **have** agreed to provide Scripps Research an aggregate of up to $ **938, 000** ~~3. 0 million~~ to fund research relating to advancing the pre- clinical development of ~~XCART~~ **our DNase oncology platform technology** . **For more information regarding** ~~The research funding was payable by us to Scripps Research on a quarterly basis in accordance with a negotiated budget, which provides for an initial payment of approximately $ 300, 000 on~~ the ~~date of the Scripps~~ Agreement ~~and subsequent quarterly payments of approximately $ 300~~ , ~~000 over a 27- month period~~ **refer to the section titled " Business Developments " above** . ~~Under the~~ **Other** ~~Scripps Agreement~~ **Agreements We** ~~, Scripps Research granted us a license within the Field (as defined in the Scripps Agreement) to any Patent Rights or Technology (as defined in the Scripps Agreement) under the terms of that certain license agreement with Scripps Research, dated February 25, 2019, assigned to us on March 1, 2019. Additionally, we~~ have **also** ~~the option to acquire a worldwide exclusive license to Scripps Research' s rights in the Technology or Patent Rights not already licensed to us, as well as a non- exclusive, royalty- free, non- transferrable license to make and use Scripps Research Technology (as defined in the Scripps Agreement) solely for the Company' s internal research purposes during the performance of the research program contemplated by the Scripps Agreement. During the second quarter of 2022, the parties mutually agreed to terminate additional funding under the Scripps Agreement. As a result, Scripps Research agreed to continue to perform work under the agreement until funding previously advanced was expended. PJSC Pharmsynthez In November 2009, we~~ entered into **various** ~~a collaborative~~ research ~~and ,~~ development **,** license **and supply** ~~agreement~~ **agreements** with ~~Pharmsynthez~~ **Serum Institute of India** (~~the~~ " ~~Pharmsynthez Arrangement~~ **Serum Institute** ") **,**

~~pursuant to which we granted an exclusive license to~~ Pharmsynthez ~~to develop, commercialize~~ and **SynBio** ~~market six product candidates based on our PolyXen and ImuXen technology in certain territories. In exchange~~ , **a wholly owned subsidiary of** Pharmsynthez ~~granted us~~ **. We** ~~an~~ **and our collaborative partners continued** ~~exclusive license to use any preclinical and clinical data developed by Pharmsynthez within the scope of the Pharmsynthez Arrangement and~~ to engage in ~~further~~ research ~~,~~ ~~development~~ and ~~commercialization of drug candidates outside of certain territories at our own expense. Pharmsynthez is wholly responsible for funding and conducting its own research and clinical~~ development activities **with** ~~in Russia. There are~~ no ~~milestones or other research~~ **resultant commercial products through December 31, 2023. No amounts were recognized as revenue** related **to** ~~payments provided for under~~ the **Serum Institute,** Pharmsynthez **or** ~~Arrangement other than royalties. The Pharmsynthez Arrangement shall continue until it is terminated in accordance with the terms and conditions set forth therein. In August 2011, we entered into a stock subscription and collaborative development agreement with~~ SynBio ~~(the " Co- Development Agreement~~ **agreements during** ~~"), a wholly- owned subsidiary of Pharmsynthez, pursuant to which we granted SynBio an exclusive license to develop, market and commercialize certain drug candidates utilizing molecules based on SynBio' s technology and our PolyXen, OncoHist and ImuXen platform technologies in Russia and the CIS, collectively referred to herein as the SynBio Market. In exchange for our granting to SynBio those certain license rights, SynBio granted an exclusive license to us to use any preclinical and clinical data generated by SynBio and to engage in the development of commercial candidates that may arise from the collaboration in any territory outside of the SynBio Market based upon the Co- Development Agreement. SynBio is wholly responsible for funding and conducting its own research and clinical development activities in Russia. There are no milestones or other research- related payments provided for under the Co- Development Agreement other than fees for the supply of~~ each ~~party' s respective research supplies based on their technology, which, when provided, are due to mutual convenience and not representative~~ of ~~an ongoing or recurring obligation to supply research supplies. Upon successful commercialization of any resultant products, we are entitled to receive a 10 % royalty on sales in certain territories and pay royalties to SynBio for sales outside those certain territories subject to the terms of the Co- Development Agreement. For~~ the years ended December 31, ~~2022~~ **2023** ~~, and December 31, 2021, there were no supply service revenues in connection with the Co- Development Agreement. The Co- Development Agreement continues until it is terminated in accordance with the terms and conditions set forth therein. Effective December 20, 2021 SynBio assigned the Co- Development Agreement to its parent company, Pharmsynthez. See Note 4 Significant Strategic Collaborations for Pharmsynthez' share ownership in us. 8 In August 2011, we entered into a collaborative research and development agreement with Serum Institute (the " Serum Agreement ") providing Serum Institute an~~ **and** ~~exclusive license to use our PolyXen technology to research and develop one potential commercial product, Polysialylated Erythropoietin (" PSA- EPO. ") Serum Institute is responsible for conducting all preclinical and clinical trials required to achieve regulatory approvals within certain predetermined territories at Serum Institute' s own expense. Royalty payments are payable by Serum Institute to us for net sales to certain customers in the Serum Institute sales territory. Royalty payments are payable by us to Serum Institute for net sales received by us over the term of the license. There are no milestone or other research- related payments due under the collaborative arrangement. The Serum Agreement continues until it is terminated in accordance with the terms and conditions set forth therein. Through December 31, 2022, no commercial products were developed and no royalty revenue or expense was recognized by us related to this arrangement. Serum Institute had a share ownership of less than 1 % of our total outstanding common stock as of December 31,~~ 2022. Our Intellectual Property We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from our collaborators or other third parties. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the U. S. and in jurisdictions outside of the U. S. covering our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know- how relating to our proprietary technology and product candidates, continuing innovation and in- licensing opportunities to develop, strengthen and maintain our proprietary position in the field of oncology. We also plan to rely on data exclusivity, market exclusivity and patent term **and supplemental patent certificate** extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to obtain and maintain licenses to use intellectual property owned by third parties; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties. Our drug candidates are in various stages of development, each protected by patent and pending patent applications in the U. S. with the U. S. Patent and Trademark Office (" USPTO ") and in certain other developed countries. Our first issued patents began to expire in 2021 with the majority of the existing issued patents for our PolyXen ~~and OncoHist~~ technology expiring between 2025 and 2030. **Our XCART and XDNASE patent families include patent applications that were recently filed, with those most recently filed having an expiration date of 2042. 8** Our patent strategy is to file patent applications on innovations and improvements in those jurisdictions that comprise the major pharmaceutical markets in the world or locations where a pharmaceutical may be manufactured. These jurisdictions generally include for our key patent portfolios, but are not limited to, the U. S., U. K., Australia, Japan, Canada, South Korea, China, India, Russia and certain other countries in the European Union (" E. U. "), though we do not necessarily file a patent application in each of these jurisdictions for every patent family. As of ~~January 23~~ **February 15** , ~~2023~~ **2024** , we directly or indirectly own (e. g. through a license with CLS), through our wholly- owned subsidiaries, Hesperix and Xenetic U. K., and Xenetic U. K.' s wholly- owned subsidiaries, Lipoxen, XTI and SymbioTec, more than 170 U. S. and international patents and pending patent applications that cover various aspects of our technologies. This number includes patents and patent applications that we have acquired or filed covering various aspects of our ~~DNase~~ **XDNASE** and XCART platform technology, including all rights throughout the world in and to patents and patent applications related to " Articles And Methods Directed To Personalized Therapy Of Cancer, " and our PolyXen

platform technology covering polysialylation and advanced polymer conjugate technologies, respectively, as well as our other product candidates. More specifically, our patents and patent applications cover cancer treatments, method of use, polymer architecture, drug conjugates, formulations, methods of manufacturing polymers and polymer conjugates along with methods of administering polymer conjugates. ~~9~~ We have received patent protection for certain therapeutics that use our PolyXen technology linking the specific therapeutic to a PSA. These include, but are not limited to, PSA- EPO, PSA- insulin and PSA- insulin like protein, a next generation Factor VIII protein product candidate SHP656 (PSA- rFVIII), PSA- DNase I and PSA- granulocyte colony stimulating factor (PSA- GCSF). Further patents cover methods to prepare proteins that are linked to a PSA **as well as covering PSA linkages** . These method patents include those that link a PSA to a protein in a high pH solution as well as patents that use a process for producing an aldehyde derivative of a sialic acid through the opening and oxidation of a sialic acid unit. For instance, we have patent protection for a PSA linkage that can be at the N- terminus. We have received patent protection for the production of PSA and the removal of endotoxin during the purification process. The removal of endotoxin occurs through the addition of a high pH solution to the PSA and a process to separate a polydisperse ionically charged polysaccharide, such as PSA, into fractions of different average molecular weight. This is accomplished through the use of a column and elution buffers with different and constant ionic strength and pH, resulting in a fractionated polysaccharide that has a molecular weight polydispersity of 1. 1 or lower. We have also received patent protection for our ~~DNase~~ **XDNASE** technology, which covers the use of DNase for the treatment of cancer and amelioration of the side effects associated with a cancer treatment. The DNase can be administered alone or in combination with a cancer therapeutic. This portfolio and that of the XCART portfolio also provide coverage for the use of certain types of CAR- T cells, with or without the addition of a DNase to treat a cancer. The portfolio further covers the use of CAR- T cells with or without ~~a~~ DNase that are administered with an immune checkpoint inhibitor or modulator to treat a cancer. Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the U. S. can provide exclusionary rights for twenty years from the earliest effective filing date. In addition, in certain instances, the term of an issued U. S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension **in the United States and supplemental patent certificate in Europe and several other countries** . The restoration period cannot be longer than five years, and the total patent term, including the restoration period, must not exceed fourteen years following FDA approval. The term of patents outside of the U. S. varies in accordance with the laws of the foreign jurisdiction but is typically also twenty years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product- by- product basis, from country- to- country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory- related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. **9** In certain situations, where we work with drugs covered by one or more patents, our ability to develop and commercialize our technologies may be affected by limitations of our access to these proprietary drugs. Even if we believe we are free to work with a proprietary drug, we cannot guarantee that we will not be accused of, or be determined to be, infringing on a third party' s rights and be prohibited from working with the drug or found liable for damages. Any such restriction on access or liability for damages would have a material adverse effect on our business, results of operations and financial condition. The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. There can be no assurance that patents that have been issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and / or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of products encompassed by our patent (s). We may have to participate in interference proceedings declared by the USPTO, which could result in a loss of the patent and / or substantial cost to us. Further, we understand that if any of our pending patent applications do not issue, or are deemed invalid following issuance, we may lose valuable IP protection. ~~10~~ U. S. and foreign patent rights and other proprietary rights exist that are owned by third parties and relate to pharmaceutical compositions and reagents, medical devices and equipment and methods for preparation, packaging and delivery of pharmaceutical compositions. We cannot predict with any certainty which, if any, of these rights will be considered relevant to our technology by authorities in the various jurisdictions where such rights exist, nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third parties. We could incur substantial costs in defending ourselves and our partners against any such claims. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the U. S. and in other countries and could result in the award of substantial damages. In the event of a claim of infringement, we or our partners may be required to obtain one or more licenses from third parties. There can be no assurance that we can obtain a license to any technology that we determine we require on reasonable terms, if at all, or that we could develop or otherwise obtain alternative technology. The failure to obtain licenses, if required, may have a material adverse effect on our business, results of operations and financial condition. Further, we may not be able to obtain IP licenses related to the development of our drug candidates on a commercially reasonable basis, if at all. It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual' s

relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information. Manufacturing and Supply We do not have the capability to manufacture our own materials necessary to support our drug candidate development programs nor do we intend to acquire such capability as part of our present business strategy. We currently have agreements in place with Catalent and Serum Institute whereby Catalent and Serum Institute would produce clinical materials for use in the development of drug candidates involving our DNase and PolyXen technologies, respectively, including candidates developed by our partners. We do not have any agreements in place to manufacture clinical materials for use in the development of our XCART technology and would seek a third party manufacturer for our clinical supply needs, if necessary. **10** Government Regulation General Government authorities in the U. S. at the federal, state and local level, and other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record- keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. Generally, a new drug must be approved by the FDA through the NDA process and a new biologic must be licensed by the FDA through the biologics license application (" BLA ") process before it may be legally marketed in the U. S. U. S. Regulation Drug Development Process In the U. S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (" FDCA "), and in the case of biologics, also under the Public Health Service Act (" PHSA "), and their implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U. S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA' s refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, warning letters or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. ~~11~~ The process required by the FDA before a drug or biologic may be marketed in the U. S. generally involves the following: · completion of preclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practices (" GLP ") regulations and other applicable regulations; · submission to the FDA of an IND, which must become effective before human clinical trials may begin; · performance of adequate and well- controlled human clinical trials in accordance with Good Clinical Practice (" GCP ") regulations to establish the safety and efficacy of the proposed drug for its intended use; · submission to the FDA of an NDA or BLA; · satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with ~~current Good Manufacturing Practices (" cGMP~~ **cGMPs** ~~")~~ requirements to assure that the facilities, methods and controls are adequate to preserve the drug' s identity, strength, quality and purity; and · FDA review and approval of the NDA or BLA. The drug or biologic manufacturer may also be subject to post- approval regulatory requirements. Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective thirty days after receipt by the FDA, unless the FDA, within the thirty- day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds may also be imposed by the FDA at any time before or during clinical trials due to safety concerns about ongoing or proposed clinical trials or noncompliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. **11** All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA if any serious and unexpected adverse events occur. An institutional review board (" IRB ") at each institution participating in the clinical trial (or in some cases an independent IRB) must review and approve each protocol before a clinical trial commences at that institution. As part of its review, the IRB must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completion and otherwise comply with IRB regulations. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined: · Phase I: The drug candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life- threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. · Phase II: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage. · Phase III: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk- benefit ratio of the drug candidate and provide, if appropriate, an adequate basis for product labeling. ~~12~~ Post- approval trials, sometimes referred to as Phase IV studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase IV clinical trials as a condition of approval of an NDA or

BLA. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB' s requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, sponsors must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life. While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA by the Sponsor, and written IND safety reports must be submitted to the FDA for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in- vitro testing suggesting a significant risk to humans and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure. There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA- regulated products are required to register and disclose specified clinical trial information, which is publicly available at www. clinicaltrials. gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. **12** U. S. Market Approval Process The results of product development, preclinical and other non- clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information will be submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees ; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews all NDAs and BLAs submitted to ensure they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in- depth substantive review. The FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP- compliant to assure and preserve the product' s identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product' s continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. ~~13~~ After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA or BLA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase III trial or other significant and time- consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase IV testing, which involves clinical trials designed to further assess a drug' s safety and effectiveness after NDA or BLA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy (" REMS ") to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve the NDA or BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for noncompliance with regulatory requirements or if problems occur following initial marketing. Orphan Drug Act The Orphan Drug Act provides incentives to manufacturers to develop and market drugs or biologics for rare diseases and conditions affecting fewer than 200, 000 persons in the U. S. at the time of application for orphan drug designation or for a patient population greater than 200, 000 in the U. S. where there is

no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the U. S. The first developer to receive FDA marketing approval for an orphan drug is entitled to a seven- year exclusive marketing period in the U. S. for that product. However, a drug that the FDA considers to be clinically superior to, or different from, another approved orphan drug, even though for the same indication, may also obtain approval in the U. S. during the seven- year exclusive marketing period. In addition, holders of exclusivity for orphan drugs are expected to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the drug. **13** Pediatric Information Under the Pediatric Research Equity Act of 2007 (" PREA "), NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the drug for the claimed indication (s) in all relevant pediatric sub- populations and to support dosing and administration for each pediatric sub- population for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan drug designation has been granted. The Best Pharmaceuticals for Children Act (" BPCA ") provides sponsors of NDAs with an additional six- month period of market exclusivity for all unexpired patent or non- patent exclusivity on all forms of the drug containing the active moiety if the sponsor submits results of pediatric studies specifically requested by the FDA under BPCA within required timeframes. The Biologics Price Competition and Innovation Act provides sponsors of BLAs an additional six- month extension for all unexpired non- patent market exclusivity on all forms of the biologic containing the active moiety pursuant to the BPCA if the conditions under the BPCA are met. ~~14~~ The Food and Drug Administration Safety and Innovation Act (" FDASIA "), which was signed into law on July 9, 2012, amended the FDCA. FDASIA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (" PSP ") within sixty days of an end- of- Phase II meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed- upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and / or other clinical development programs. Expedited Development and Review Programs The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life- threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast Track product at any time during the clinical development of the product. For a Fast Track designated product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life- threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well- controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well- controlled post- marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre- approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post- marketing restrictions as it deems necessary to assure safe use of the drug, such as (i) distribution restricted to certain facilities or physicians with special training or experience or (ii) distribution conditioned on the performance of specified medical procedures. **14** FDASIA established a new category of drugs and biologics referred to as " breakthrough therapies " that may be eligible to receive Breakthrough Therapy Designation. A sponsor may seek FDA designation of a drug or biologic candidate as a " breakthrough therapy " if the product is intended, alone or in combination with one or more other products, to treat a serious or life- threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will expedite the development and review of such drug. All requests for breakthrough therapy

designation will be reviewed within 60 days of receipt, and the FDA will either grant or deny the request. ~~15~~ The 21st Century Cures Act, enacted in 2016, established a new expedited approval program for regenerative medicine products, including cell and gene therapies. The Regenerative Medicine Advanced Therapy (“ RMAT ”) program established an expedited review program to facilitate development and review of regenerative medicine therapies intended to address an unmet medical need in patients with serious conditions. An investigational drug is eligible for RMAT designation if: (1) It meets the definition of regenerative medicine therapy (such as a cell therapy or gene therapy); (2) it is intended to treat, modify, reverse, or cure a serious condition; and (3) preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition. Advantages of the RMAT designation include all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with FDA. Post- Approval Requirements Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements or standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug and biologics manufacturers and other entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. U. S. Patent Term Restoration and Marketing Exclusivity The Biologics Price Competition and Innovation Act, or BPCIA, amended the Public Health Service Act to authorize the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. A competitor seeking approval of a biosimilar must file an application to establish its molecule as highly similar to an approved innovator biologic, among other requirements. The BPCIA, however, bars the FDA from approving biosimilar applications based on the Company’ s data for twelve years after an innovator biological product receives initial marketing approval. This twelve- year period of data exclusivity may be extended by six months, for a total of twelve and a half years, if the FDA requests that the innovator company conduct pediatric clinical investigations of the product. Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch- Waxman Amendments. The Hatch- Waxman Amendments 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. However, patent term extension cannot extend the remaining term of a patent beyond a total of fourteen years from the product’ s approval date. The patent term extension period is generally one- half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application up to a maximum of five years extension. Only one patent applicable to an approved drug is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for extension of the patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date where reasonably obtainable and depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA. ~~16~~ **15** Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five- year period of non- patent marketing exclusivity within the U. S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505 (b) (2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non- infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA or supplement to an existing NDA if new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application (e. g., new indications, dosages or strengths of an existing drug). This three- year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five- year and three- year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness. Pediatric exclusivity is another type of regulatory market exclusivity in the U. S. under the BPCA. Pediatric exclusivity provides for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children as addressed in the section named “ Pediatric Information ” above. In addition, orphan drug exclusivity, as described above, may offer a seven- year period of marketing exclusivity, except in certain circumstances. Foreign Regulation In addition to regulations in the U. S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our drug candidates. Whether or not we obtain FDA approval for our drug candidates, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the drug candidates in those countries. Certain countries outside of the U. S. have a similar process that requires the submission of a clinical trial application (“ CTA ”) much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country’ s national health authority and an independent ethics committee, much like

the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country' s requirements, clinical study development may proceed. The requirements and process governing the conduct of clinical trials, product approval and licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the NDA or BLA in the U. S. is similar to that required in the European Union, with the exception of, among other things, country- specific document requirements. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator' s data to assess a generic application. During the additional two- year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator' s data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union' s regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. ~~17~~ **16** The criteria for designating an " orphan medicinal product " in the European Union are similar in principle to those in the U. S. Under Article 3 of Regulation (EC) 141 / 2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10, 000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847 / 2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The 10- year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, marketing authorization may be granted to a similar product for the same indication at any time if: · the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; · the applicant consents to a second orphan medicinal product application; or · the applicant cannot supply enough orphan medicinal products. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing or approval, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Other Regulatory Matters Manufacturing, sales, promotion and other activities following product approval are also potentially subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the U. S., the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the U. S., sales, marketing and scientific / educational programs must also comply with state and federal fraud and abuse laws, including state and federal anti- kickback, false claims, data privacy and security and physician payment transparency laws. Pricing and rebate programs must comply with the federal health care program (e. g. Medicaid) rebate requirements of the U. S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, as well as the Inflation Reduction Act of 2022. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U. S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child- resistant packaging requirements under the U. S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws. ~~18~~ The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. **17** The failure to comply with regulatory requirements may subject us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or

withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. Reimbursement In both domestic and foreign markets, sales and reimbursement of any approved products will depend, in part, on the extent to which the costs of such products will be covered by third- party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third- party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. The containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost- containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. For example, in the U. S. there have been several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drugs. Additionally, in May 2018, the Trump Administration laid out a " Blueprint " to lower drug prices and reduce out- of- pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out- of- pocket costs of drug products paid by consumers. While the Biden Administration has not continued this effort, it has the authority to institute other actions. In December of 2020, the Trump Administration issued interim final rules focused on attempting to lower drug prices, including permitting the importation of certain drugs from Canada, most- favored nation pricing for certain drug categories under Medicare Part B and modifications to the Medicare Part D drug rebate program by modifying the U. S. federal Anti- Kickback Statute. The Part B most- favored nation rule was blocked from taking effect on January 4, 2021, by a federal judge stating that the rule was rushed and the public was not provided time to give comment as required by the Administrative Procedures Act. Then, on December 29, 2021, CMS issued a final rule that formally rescinded the most- favored nation rule. There is also pending litigation to stay the changes to the Medicare Part D drug rebate program and the Anti- Kickback Statute. On January 30, 2021, the District Court for the District of Columbia granted the parties' stipulated request to delay the effective date of the Part D rebate rule to January 1, 2023. On August 7, 2022, Congress passed the Inflation Reduction Act of 2022 which delayed the implementation of the changes to the Medicare Part D drug rebate program and the U. S. Federal Anti- Kickback Statute until January 2032. Additionally, the Inflation Reduction Act of 2022 may impact existing Medicare programs that cover prescription drugs. In addition to other relevant provisions, the Inflation Reduction Act of 2022 allow the Medicare program to directly negotiate the price of certain high- expenditure prescription drugs covered under Medicare Parts B and D, starting in the year 2028 and 2026, respectively, by setting certain" maximum fair prices." Moreover, the Inflation Reduction Act of 2022 requires manufacturers to pay rebates to the federal government if prices of certain drugs covered under the Medicare program rise faster than the rate of inflation. ~~19~~ At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. **18** Within the U. S., if we obtain appropriate approval in the future to market any of our product candidates, we may seek approval and coverage for those products under Medicaid, Medicare and the Public Health Service, or PHS, pharmaceutical pricing program and may also seek to sell the products to federal agencies. Medicaid is a joint federal and state program that is administered by the states for low- income and disabled beneficiaries. Under the Medicaid Drug Rebate Program, manufacturers are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation. Medicare is a federal program administered by the federal government that covers individuals age 65 and over as well as those with certain disabilities. Medicare Part D provides coverage to enrolled Medicare patients for self- administered drugs (i. e., drugs that do not need to be administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U. S. government, and each drug plan **and / or pharmacy benefit manager** establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan **and / or pharmacy benefit manager** may modify from time- to- time. Medicare Part B covers most injectable drugs given in an in- patient setting and some drugs administered by a licensed medical provider in hospital outpatient departments and doctors' offices. Medicare Part B is administered by Medicare Administrative Contractors, which generally have the responsibility of making coverage decisions. Subject to certain payment adjustments and limits, Medicare generally pays for Part B covered drugs based on a percentage of manufacturer- reported average sales price. Drug products are subject to discounted pricing when purchased by federal agencies via the Federal Supply Schedule, or FSS. FSS participation is required for a drug product to be covered and paid for by certain federal agencies and for coverage under Medicaid, Medicare Part B and the PHS pharmaceutical pricing program. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended to not exceed the price that a manufacturer charges its most- favored non- federal customer for its product. In addition, prices for drugs purchased by the Veterans Administration, Department of Defense (including drugs purchased by military personnel and dependents through the TRICARE retail pharmacy program), Coast Guard and PHS are subject to a cap on pricing (known as the " federal ceiling price ") and may be subject to an additional discount if pricing increases more than inflation. To maintain coverage of drugs under the Medicaid Drug Rebate Program, manufacturers are required to extend discounts to certain purchasers under the PHS pharmaceutical pricing program. Purchasers eligible for discounts include hospitals that serve a disproportionate share of financially- needy patients, community health clinics and other

entities that receive health services grants from the PHS. In March 2010, the U. S. Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act, or the Affordable Care Act, which included changes to the coverage and payment for drug products under government health care programs. Since its enactment, there have been judicial and Congressional challenges to numerous elements of the Affordable Care Act, as well as efforts by both the executive and legislative branches of the federal government to repeal or replace certain aspects of the Affordable Care Act. For example, the former President Trump signed Executive Orders designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. In addition, the U. S. Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the Affordable Care Act, such as removing penalties, starting January 1, 2019, for not complying with the Affordable Care Act' s individual mandate to carry health insurance, delaying the implementation of certain mandated fees and increasing the point- of- sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. In December 2018, a Texas U. S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the " individual mandate " was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017, or the Tax Act. Although the Supreme Court ruled the plaintiffs did not have standing in June of 2021, any other executive, legislative or judicial action to " repeal and replace " all or part of the Affordable Care Act may have the effect of limiting the amounts that government agencies will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure, or may lead to significant deregulation, which could make the introduction of competing products and technologies much easier. Regardless of the future of the Affordable Care Act provisions, the Congress will continue to debate a range of policies that could impact the prices pharmaceutical companies charge for products or how much they are reimbursed. ~~20~~ **19** Environmental Regulation In addition to being subject to extensive regulation by the FDA, we must also comply with environmental regulation insofar as such regulation applies to us or our drug candidates. Our costs of compliance with environmental regulation as applied to similar pharmaceutical companies are minimal, since we do not currently, nor do we intend to, engage in the manufacturing of any of our drug candidates. We currently use unaffiliated manufacturers to produce all of our drug candidate material and receive final material from such manufacturer, without any involvement on our part in the manufacturing process at any stage of the process. Although we believe that our safety procedures for using, handling, storing and disposing of our drug candidate materials comply with the environmental standards required by state and federal laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We do not carry a specific insurance policy to mitigate this risk to us or to the environment. Employees At December 31, ~~2022~~ **2023** , we employed four full- time employees. We are not a party to any collective bargaining agreement with our employees, nor are any of our employees a member of any labor unions. To complement our own professional staff, we utilize specialists in regulatory affairs, pharmacovigilance, process engineering, manufacturing, quality assurance, preclinical and clinical development, accounting and business development. These individuals include scientific advisors as well as independent consultants. The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. The key competitive factors affecting the success of all our product candidates, if approved, are likely to be their efficacy, safety, side effects, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third- party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third- party payors seeking to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products. ~~21~~ **20** The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy, immunotherapy, and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. To the extent our product candidates are ultimately used in combination with or as an adjunct to existing drug or other therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third- party payors. In general, although there has been

considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high. DNase for pancreatic cancer and solid tumors In the field of pancreatic cancer, we will compete with the few, currently approved treatments for pancreatic carcinoma, including pancreatic ductal adenocarcinoma (“ PDAC ”). In the first line setting, Gemcitabine in combination with Abraxane ® or FOLFIRINOX regimen are the current standard of care **, although NALIRIFOX, which substitutes liposomal irinotecan (Onivyde) for irinotecan, recently received FDA approval for first-line treatment of metastatic pancreatic adenocarcinoma** . Oncologists have limited options of existing therapies for second-line metastatic patients. The only FDA- approved second- line treatment is Onivyde ® in combination with Fluorouracil (5FU) and leucovorin (LV) for gemcitabine- treated patients. In addition to chemotherapy, Merck’ s KEYTRUDA ® was approved for MSI- H cancers (approximately 1 % of all cases) and Lynparza ® was approved for maintenance of BRCA **(or “ BReast CAncer gene ”)** mutated pancreatic cancer (approximately 7 % of all cases). In the last years there have been a number of late-stage clinical failures of compounds for advanced PDAC. Most of these failed trials have been based on a single promising endpoint. There are very few compounds in advanced stages of development in PDAC. With respect to other solid tumors, there are a large number of companies developing treatments intended to be used in combination with approved immunotherapies, including immune checkpoint inhibitors, to treat a variety of solid tumor indications. ~~XCART for B- cell lymphomas There are a number of CAR T therapies approved in the U. S. and EU including Novartis’ Kymriah (tisagenlecleucel); Gilead Sciences, Inc.’ s and Kite Pharma’ s Yescarta (axicabtagene ciloleucel) and Tecartus (brexucabtagene autoleucel); Bristol Myers Squibb’ s Breyanzi (lisocabtagene maraleucel) and Abecma (idecabtagene vicleucel); and Janssen’ s Carvykti (ciltacabtagene autoleucel).~~ In ~~addition~~ **the field of CRC** , there are ~~over one~~ **numerous approved treatments for CRC diagnosed at earlier stages. However, for mCRC, chemotherapy remains the mainstay of systemic treatment for MSS / MMRp mCRC, which at 95 %, represent the majority of mCRC patients. Chemotherapy regimens will typically consist of a fluoropyrimidine (5** - ~~hundred CAR T~~ **FU or capecitabine) paired in a two- drug regimen (doublet) with irinotecan or oxaliplatin. Treatment regimens can be 5- FU- or capecitabine- based and can be either oxaliplatin- based (FOLFOX or CAPEOX) or irinotecan- based (FOLFIRI or CAPIRI) with no difference in survival. Regimens with a three- drug (triplet) combination, FOLFIRINOX or FOLFOXIRI, are also available as first- line** therapy ~~products in development~~ **and are commonly paired** with **the anti** ~~a significant number being allogeneic and off~~ - ~~the~~ **VEGF antibody bevacizumab. Second** - ~~shelf cell~~ **line therapy is tailored according to previous** therapies. In ~~addition~~ **general** , **patients who receive oxaliplatin-based chemotherapy upfront should be treated with irinotecan- based chemotherapy** ~~depending on the diseases that our CAR T therapies target, we may face competition in the indication of interest from both CAR T therapies~~ and ~~other modalities~~ **vice versa [20 – 22]. Biologics** such as **aflibercept ramucirumab are added based on molecular profiling. After progression on second- line therapy, patients with RAS / BRAF wild- type disease receive an EGFR inhibitor combined with irinotecan. Alternatively, if they have HER2 mutation, trastuzumab is typically preferred. Patients with the BRAFV600E mutation typically receive an encorafenib- cetuximab regimen. For those 5 % of patients with MSI- H / dMMR mCRC, immune checkpoint inhibitors are now the preferred first line therapy. However, 50 % of those will fail and the therapeutic options then become very limited. Immunotherapy is so far largely considered ineffective in MSS / MMRp mCRC. We will compete with novel combinations of ICIs with conventional cancer drugs or immunotherapeutics that have started to expose vulnerabilities in MSS / MMRp mCRC. These include dual immune checkpoint inhibition of both the PD- 1 / L1 axis and CTLA- 4. Other combinations being explored include immunotherapies combined with anti- EGFR antibodies,** small ~~molecules~~ - **molecule VEGFR inhibitors, small molecule inhibitors against other targets (for example, KRAS),** and ~~antibodies~~ **novel ICIs targeting lymphocyte activation gene 3 (LAG3)** . ~~T~~ **These combination have shown modest benefit and with the exception of LAG3, do not directly address the main reasons for ICI failure, which are lower mutation and neoantigen loads in MSS / MMRp mCRC compared to MSI - H / MMRd mCRC** ~~cell based treatments for cancer~~ , ~~such as CAR T and TCR therapies, have recently been an~~ **and immunosuppression** ~~area of significant research and development by academic institutions and biopharmaceutical companies~~ . **21** PSA for Drug Delivery Current competing platforms include PEGylation, Fc- fusion, albumin- fusion, HESylation, PASylation, and CTP- fusion, among others as well as those of academic institutions and other smaller pharmaceutical companies engaged in drug development. In addition to competing with universities and other research institutions in the development of drug products, therapies, technologies and processes, we may compete with other companies in acquiring rights to products or technologies from universities. ~~22~~ Available Information Our website address is www. xeneticbio. com. The information on, or that can be accessed through, our website is not part of this Annual Report on Form 10- K. Our Annual Reports on Form 10- K, Quarterly Reports on Form 10- Q and Current Reports on Form 8- K and amendments to those reports are available, free of charge, on or through our website as soon as practicable after we electronically file such forms, or furnish them to, the SEC. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding our filings at www. sec. gov. In addition to disclosing current information pursuant to Section 13 or 15 (d) of the Exchange Act and for reports of information required to be disclosed by Regulation FD through our SEC filings, we also intend to disclose such current information through our investor relations website, press releases, public conference calls and webcasts. **22** ITEM 1A – RISK FACTORS Our business is subject to numerous risks. You should consider carefully the risks and uncertainties described below, in addition to other information contained in this Annual Report as well as our other public filings with the Securities and Exchange Commission. Any of the following risks could have a material adverse effect on our business, financial condition, results of operations and prospects and cause the trading price of our common stock to decline. Risks Related to Our Financial Condition and Capital Requirements We have never been profitable and may never achieve or sustain profitability. If we are unable to generate sufficient revenue from our operations to pay expenses or we are unable to

obtain additional financing on commercially reasonable terms, our business, financial condition and results of operations may be materially and adversely affected. We are a clinical- stage biopharmaceutical company with a limited operating history. Pharmaceutical product and technology development is a highly speculative undertaking and involves a substantial degree of risk. We have no products approved for commercial sale and have generated only limited revenue to date. **Our** ~~Prior to April 2022, we focused primarily on pre- clinical development efforts associated with our XCART technology. With the licensing of the DNase oncology platform from CLS in April 2022, our~~ primary focus is now on advancing ~~that technology~~ **our DNase oncology platform** via partnering opportunities or through regulatory approval and commercialization. We expect to continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we have never been profitable and we may not achieve profitability in the foreseeable future, if at all. Our ability to generate profits in the future will depend on a number of factors, including: · Funding the costs relating to the research and development, regulatory approval, commercialization and sale and marketing of our drug candidates and technologies; · Market acceptance of our drug candidates and technologies; · Costs of acquiring and developing new drug candidates and technologies; · Ability to bring our drug candidates to market; · General and administrative costs relating to our operations; · Increases in our research and development costs; · Charges related to purchases of technology or other assets; · Establishing, maintaining and protecting our intellectual property rights; · Attracting, hiring and retaining qualified personnel; and · Our ability to raise additional capital. ~~23~~ As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of approximately $ ~~189~~ **193** . ~~1~~ **2** million. We expect to incur additional significant operating losses as we expand our research and development activities and our commercialization, marketing and sales efforts. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our current drug candidates may not achieve the clinical endpoints of applicable trials, we are unable to predict the timing or amount of increased expenses and if or when we will achieve or maintain profitability. If we are unable to generate sufficient revenue from our operations to pay expenses or we are unable to obtain additional financing on commercially reasonable terms, our business, financial condition and results of operations may be materially and adversely affected. **23** We will require substantial additional funding to achieve our goals. Failure to obtain this necessary capital when needed on acceptable terms, or at all, may force us to delay, limit or terminate our product development efforts, other operations or commercialization efforts. Developing drug candidates is an expensive, risky and lengthy process, and we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our drug candidates. As of December 31, ~~2022~~ **2023** , we had cash of approximately $ ~~13~~ **9** . ~~1~~ **0** million. We expect that we will require additional capital to commence and complete clinical trials, obtain regulatory approval for, and to commercialize, our drug candidates, including our other preclinical drug candidates and our future drug candidates. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Additional funding may come through public or private equity or debt financings, third- party funding, marketing and distribution arrangements or other collaborations, strategic alliances and licensing arrangements (or a combination of these approaches). In any event, we will require additional capital to pursue preclinical and clinical activities, pursue regulatory approval for, and to commercialize, our longer term pipeline drug candidates. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. Our ability to raise additional funds will depend on financial, economic, political, and market conditions and other factors over which we may have no or limited control. Market volatility resulting from **economic, political** ~~the ongoing COVID- 19 pandemic~~ or other factors, such as geopolitical tension, including the **conflicts in the** ~~recent Russian invasion of~~ Ukraine **and the Middle East** , and any resulting sanctions, export controls or other restrictive actions, could also adversely impact our ability to access capital as and when needed. Additional funds may not be available when we need them, on terms and at a cost that are acceptable to us, or at all. Any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our drug candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may negatively impact the holdings or the rights of our stockholders, and the issuance of additional securities (whether equity or debt) by us, or the possibility of such issuance, may cause the market price of our shares to decline. The incurrence of indebtedness could result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue our pre- clinical development program or the commercialization of any drug candidates. We may also be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could harm our business, financial condition and results of operations. ~~24~~ Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings, as well as selectively continuing to enter into collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, equity interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Such debt financing may also be secured by all or a portion of our assets. If we raise funds by selectively continuing to enter into collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish additional valuable rights to our

technologies, future revenue streams, research programs or drug candidates, or we may have to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves. If we are unable to raise additional funds through collaborations, strategic alliances or licensing arrangements, we may be required to terminate product development or future commercialization efforts or to cease operations altogether. **24** Risks Related to the Discovery and Development of our Pharmaceutical Products Our business is substantially dependent on the success of the DNase oncology platform. Our business will substantially depend on the successful clinical development, regulatory approval and commercialization of the DNase oncology platform. It will require substantial clinical development and regulatory approval efforts before we are permitted to commence its commercialization, if ever. We have, and plan to continue to pursue our clinical development strategy through academic and strategic collaborations. If we have difficulty maintaining, obtaining, or are unable to obtain these collaborations and additional academic collaborations as planned, we may need to delay, limit or terminate any ongoing or planned clinical development, which would have an adverse effect on our business. The clinical trials and manufacturing and marketing of DNase and any other product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the U. S., the European Union and other jurisdictions where we intend to test and, if approved, market our product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication and potentially in specific patient populations. This process can take many years and may include post- marketing studies and surveillance, which would require the expenditure of substantial resources beyond the proceeds we have currently raised. Of the large number of drugs in development for approval in the U. S. and the European Union, only a small percentage successfully complete the FDA or European Medicines Agency regulatory- approval processes, as applicable, and are commercialized. Accordingly, even if we are able to obtain the requisite financing or identify an academic or strategic collaboration partner to continue to fund our research, development and clinical programs, we cannot assure you that DNase or any of our other product candidates will be successfully developed or commercialized. ~~25~~ We are an early stage company in the business of developing pharmaceutical products including drug candidates and technologies. Given the uncertainty of such development, our business operations may never fully materialize and create value for investors. We have invested substantially all of our efforts and financial resources in developing our products, and we currently do not have any products that have gained marketing approval. Our revenues **currently** ~~to date~~ consist primarily of ~~collaboration and~~ royalty revenue from a single partner and not from product sales. Our ability to generate product revenues, which may not occur for several **more** years, if ever, will depend on the successful development and eventual commercialization of our drug candidates. We currently generate royalty revenue under a sub- license agreement but do not have revenue from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. Each of our drug candidates will require development, management of development and manufacturing activities, marketing approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenues from drug sales. We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly- evolving fields, particularly in the pharmaceutical area. For example, to execute our business plan we will need to successfully: · Execute development activities for our drug candidates, including successful enrollment in and completion of clinical trials; · Obtain required marketing approvals for the development and commercialization of our drug candidates; · Obtain and maintain patent and trade secret protection or regulatory exclusivity for our drug candidates; · Protect, leverage and expand our intellectual property portfolio; · Establish and maintain clinical and commercial manufacturing capabilities or make arrangements with third- party manufacturers for clinical and commercial manufacturing; · Build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners, if our drug candidates are approved; · Gain acceptance for our drug candidates, if approved, by patients, the medical community and third- party payors; · Effectively compete with other therapies; · Obtain and maintain healthcare coverages and adequate reimbursement; · Maintain a continued acceptable safety profile for our drug candidates following approval; · Develop and maintain any strategic relationships we elect to enter into, if any; · Enforce and defend intellectual property rights and claims; and · Manage our spending as costs and expenses increase due to preclinical development, clinical trials, marketing approvals and commercialization. **25** We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our pharmaceutical products. Identifying and qualifying patients to participate in clinical studies of our pharmaceutical products is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit patients to participate in testing our pharmaceutical products. We may experience delays. If patients are unwilling to participate in our clinical studies because of negative publicity from adverse events in the biopharmaceutical industries or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether. ~~26~~ We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient enrollment is affected by many factors, including: · Severity of the disease under investigation; · Real or perceived availability of alternative treatments; · Size and nature of the patient population; · Eligibility criteria for and design of the trial in question; · Perceived risks and benefits of the drug candidate under study; · Proximity and availability of clinical sites for prospective patients; · Ongoing clinical trials of potentially competitive agents; · Physicians' and patients' perceptions as to the potential advantages of our drug candidates being studied in relation to available therapies or other products under development; · Our CRO' s and our trial sites' efforts to facilitate timely enrollment in clinical trials; · Patient referral practices of physicians; and · The need to

monitor patients and collect patient data adequately during and after treatment. We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by the FDA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical study in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including: · Difficulty in establishing or managing relationships with CROs and physicians; · Different standards for the conduct of clinical studies; · Our inability to locate qualified local consultants, physicians and partners; and · The potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment. If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which would have an adverse effect on our business. ~~27~~ **26** We may encounter substantial delays in commencement, enrollment or completion of our clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing our current and future drug candidates on a timely basis, if at all. Before obtaining marketing approval from regulatory authorities for the sale of our current and future drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug candidates. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include: · Delays in reaching a consensus with regulatory agencies on study design; · Delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites; · Delays in obtaining required IRB, or Independent Ethics Committee approval at each clinical study site; · Delays in recruiting suitable patients to participate in our clinical studies; · Imposition of a clinical hold by regulatory agencies, including after an inspection of our clinical study operations or study sites; · Failure by our CROs, other third parties or us to adhere to clinical study requirements; · Failure to perform in accordance with the FDA' s GCP or applicable regulatory requirements in other countries; · Delays in the testing, validation, manufacturing and delivery of our drug candidates to the clinical sites; · Delays in having patients complete participation in a study or return for post- treatment follow- up; · Clinical study sites or patients dropping out of a study; · Clinical trial results may fail to demonstrate the safety and / or efficacy of the drug candidate; · Occurrence of serious adverse events associated with the drug candidate that are viewed to outweigh its potential benefits; or · Changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our drug candidates, we may need to conduct additional studies to bridge our modified drug candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our drug candidates and may harm our business, financial condition, results of operations and prospects. If the results of our clinical studies are inconclusive or if there are safety concerns or adverse events associated with our pharmaceutical products, we may: · Be delayed in obtaining marketing approval or licenses for our drug candidates, if we receive them at all; · Obtain approval for indications or patient populations that are not as broad as intended or desired; · Obtain approval with labeling that includes significant use or distribution restrictions or safety warnings; · Be subject to changes with the way the product is administered; · Be required to perform additional clinical studies to support approval or be subject to additional post- marketing testing requirements; · Have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy; · Be subject to the addition of labeling statements, such as warnings or contraindications; · Be sued; or · Experience damage to our reputation. As described above, any of these events could prevent us from achieving or maintaining market acceptance **and approval** of our pharmaceutical products and impair our ability to generate revenues. ~~28~~ **27** If we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a drug candidate, or the approval may be for a more narrow indication than we expect. A drug candidate cannot be commercialized until the appropriate regulatory authorities have reviewed and approved the drug candidate. Even if our drug candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory advisory group or authority recommends non- approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a drug candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post- marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our drug candidates. Failure to obtain, or a delay in obtaining, regulatory approval to commercialize a drug candidate will impair our ability to generate revenues and harm our business prospects. If we obtain regulatory approval for a drug candidate, our drug candidate will remain subject to regulatory scrutiny. If our drug candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, **reporting,** conduct of post- marketing studies and submission of safety, efficacy and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. Manufacturers and manufacturing facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA or marketing authorization application (" MAA "). Accordingly, we and our collaborators and suppliers must continue to expend time, money and effort in all areas of regulatory

compliance, including manufacturing, production and quality control. Any regulatory approvals that we or our collaboration partners receive for our drug candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval or may contain requirements for potentially costly additional clinical trials and surveillance to monitor the safety and efficacy of the drug candidate. We will be required to report certain adverse reactions **,** **serious adverse events** and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety or other issues related to regulatory review and approval could result in delays in product development or commercialization or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product' s approved label. As such, we are not allowed to promote our products for indications or uses for which they do not have approval. If our drug candidates are approved, we must submit new or supplemental applications and obtain approval for certain changes to the approved products, product labeling or manufacturing process. We could also be asked to conduct post- marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. An unsuccessful post- marketing study or failure to complete such a study could result in the withdrawal of marketing approval. ~~29~~ **28** If a regulatory agency discovers previously unknown problems with an approved product, such as adverse events of unanticipated severity or frequency or problems with our manufacturing facilities, or if a regulatory agency disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things: · Issue **inspectional findings; · Issue** untitled and warning letters; · Impose civil or criminal penalties; · Suspend or withdraw regulatory approval or revoke a license; · Suspend or hold any of our ongoing clinical trials; · Refuse to approve pending applications or supplements to approved applications submitted by us; · Impose restrictions on our operations, including closing our manufacturing facilities; or · Seize or detain products or require a product recall. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of the Company and our operating results will be negatively impacted. The commercial success of any current or future pharmaceutical products will depend upon the degree of market acceptance by physicians, patients, third- party payors and others in the medical community. Even with the requisite approvals, the commercial success of our pharmaceutical products will depend in part on the medical community, patients and third- party payors accepting our pharmaceutical products as medically useful, cost- effective and safe. Any pharmaceutical product that we, or our partners, bring to the market may not gain market acceptance by physicians, patients, third- party payors or others in the medical community. The degree of market acceptance of these pharmaceutical products, if approved for commercial sale, will depend on a number of factors, including: · The effectiveness of our approved drug candidates as compared to currently available products; · Patient willingness to adopt our approved drug candidates in place of current therapies; · Our ability to provide acceptable evidence of safety and efficacy; · Relative convenience and ease of administration; · The prevalence and severity of any adverse side effects; · Restrictions on use in combination with other products; · Availability of alternative treatments; · Pricing and cost-effectiveness assuming either competitive or potential premium pricing requirements, based on the profile of our drug candidates and target markets; · Effectiveness of our or our partners' sales and marketing strategy; · Our ability to obtain sufficient third-party coverage or reimbursement; and · Potential product liability claims. Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third- party payors on the benefits of the pharmaceutical products may require a significant amount of resources and may never be successful. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. ~~30~~ **29** The commercial potential of a pharmaceutical candidate in development is difficult to predict. If the market size for a new drug candidate or technology is significantly smaller than we anticipate, it could significantly and negatively impact our revenue, results of operations and financial condition. It is very difficult to estimate the commercial potential of pharmaceutical products due to important factors, such as safety and efficacy compared to other available technologies or treatments, including changing standards of care, third-party payor reimbursement standards, patient and physician preferences, the availability of competitive alternatives that may emerge either during the long drug development process or after commercial introduction and the availability of generic versions of our successful drug candidates following approval by government health authorities, based on the expiration of regulatory exclusivity or our inability to prevent generic versions from coming to market by asserting our patents. If due to these factors, or others, the market potential for a pharmaceutical product is lower than we anticipated, it could significantly and negatively impact the commercial terms of any collaboration partnership potential for such pharmaceutical product or, if we have already entered into a collaboration for such pharmaceutical product, the revenue potential from royalty and milestone payments could be significantly diminished, which would negatively impact our business, financial condition and results of operations. Failure to obtain or maintain adequate coverage and reimbursement for our drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. The success of our drug candidates, if approved, depends on the availability of adequate coverage and reimbursement from third- party payors. In addition, because our drug candidates represent new approaches to the treatment of certain diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our drug candidates or assure that coverage and reimbursement will be available for any product that we may develop. Patients who are provided medical treatment for their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from ~~governmental~~ **federal** ~~healthcare~~ ---- **health care** programs, such as Medicare and Medicaid, and

commercial payors are critical to new product acceptance. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, **as well as their pharmacy benefit managers** 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. In the United States, no uniform policy of coverage and reimbursement for products exists among third- party payors and their contracted pharmacy benefit managers that manage prescription benefits for such payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third- party payor is a time- consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor- by- payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co- payments that patients find unacceptably high. Additionally, third- party payors and their pharmacy benefit managers may not cover, or provide adequate reimbursement for, long- term follow- up evaluations **that may be** required **for** ~~following the use of~~ our ~~gene- modifying~~ products. Patients are unlikely to use our drug candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our drug candidates **and / or if patient out- of- pocket costs (such as co- pays or co- insurance) are prohibitively high** . There is significant uncertainty related to insurance coverage and reimbursement of newly- approved products. It is difficult to predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our drug candidates. ~~31~~ **30** Moreover, increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly-approved products and, as a result, they may not cover or provide adequate payment for our drug candidates. We expect to experience pricing pressures in connection with the sale of any of our drug candidates due to the trend toward managed healthcare **, value- based pricing** , the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes. We intend to seek approval to market our drug candidates in both the United States and in select foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our drug candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, the pricing of pharmaceutical products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our drug candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a drug candidate. In addition, market acceptance and sales of our drug candidates will depend significantly on the availability of adequate coverage and reimbursement from third- party payors for our drug candidates and may be affected by existing and future health care reform measures. Failure to obtain or maintain adequate coverage and reimbursement for our drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. We may use our financial and human resources to pursue a particular research program or drug candidate and fail to capitalize on programs or drug candidates that may be more profitable or for which there is a greater likelihood of success. Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs, drug candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for drug candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate, or we may allocate internal resources to a drug candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement. Failure to pursue opportunities with greater commercial potential or relinquishing valuable rights to drug candidates may adversely impact our business, results of operations and prospects. We may not be successful in our efforts to identify or discover additional pharmaceutical products. The success of our business depends primarily upon our ability to identify and develop pharmaceutical products. Our research programs may fail to identify potential pharmaceutical products for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential pharmaceutical products, or our potential pharmaceutical products may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new pharmaceutical products require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or pharmaceutical products that ultimately prove to be unsuccessful. If we are not successful in our efforts to identify or discover additional pharmaceutical products, it could adversely affect our business, results of operations and prospects. ~~32~~ **31** The market opportunities for our drug candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small. Cancer therapies are sometimes characterized as first line, second line or third line, and the FDA often approves new therapies initially only for third line use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, which usually consists of chemotherapy, hormone therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecules or a combination of these. Third line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery and new technologies. In markets with approved therapies, we expect to initially seek approval of our drug candidates as a later stage therapy for patients who have failed other approved treatments. Subsequently, for those drugs that prove to be

sufficiently beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our drug candidates, even if approved, would be approved for second line or first line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second line or first line therapy. Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our drug candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. In addition, the potentially addressable patient population for our drug candidates may be limited or may not be amenable to treatment with our drug candidates. Even if we obtain significant market share for our drug candidates, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first or second line therapy, which may adversely affect our business and results of operations. Clinical trials may fail to demonstrate the safety and efficacy of our pharmaceutical drug candidates and could prevent or significantly delay regulatory approval. Before receiving NDA or BLA approval to commercialize a drug candidate, we must demonstrate to the FDA, with substantial evidence from well-controlled clinical trials, that the drug candidate is both safe and effective or the biologic is safe, pure and potent. If these trials or future clinical trials are unsuccessful, our business and reputation could be harmed and our stock price could be adversely affected. Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any of our current and future collaborators may decide, or regulators may require us, to conduct additional clinical or preclinical testing. We will be required to demonstrate with substantial evidence through well- controlled clinical trials that our drug candidates are as safe and effective for use in a specific patient population as the respective reference products before we can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that future larger registration clinical trials will be successful because drug candidates in later- stage clinical trials may fail to demonstrate equivalent safety and efficacy to the satisfaction of the FDA and foreign regulatory agencies despite having progressed through initial clinical trials. Drug candidates that have shown promising results in early clinical trials may still fail in subsequent confirmatory clinical trials. Similarly, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval. In some instances, there can be significant variability in safety or efficacy results between different trials of the same drug candidate due to numerous factors, including but not limited to, changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and the rate of dropout among clinical trial participants. Because of these risks, our research and development efforts, and those of our collaborative partners, may not result in any commercially viable products. If a significant portion of these development efforts is not successfully completed, or if required regulatory approvals are not obtained by us or our partners, or any approved products are not commercially successful, we may not generate significant revenues or become profitable. ~~33~~ **32** We may fail to obtain orphan drug designations from the FDA for our drug candidates, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200, 000 in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic 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. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. We may seek to obtain orphan drug designation for our active drug candidates for any qualifying indications they may be approved for in the future. Even if we obtain such designations, we may not be the first to obtain marketing approval of our drug candidate for the orphan- designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan- designated indication, or 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 quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, even if we seek orphan drug designation for our drug candidates, we may never receive such designations. Healthcare legislative reform measures may have a material adverse effect on our business and results of operations. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory enactments in recent years that change the

healthcare system in ways that could impact our future ability to sell our drug candidates profitably. Furthermore, there have been and continue to be a number of initiatives at the federal and state level that seek to reduce healthcare costs. Most significantly, in March 2010, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the " ACA "), was signed into law, which includes measures that significantly change the way healthcare is financed by both governmental and private insurers. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. In addition, on January 20, 2017, former President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Further, on October 12, 2017, former President Trump issued another executive order requiring the Secretaries of HHA and the Departments of Labor and Treasury to consider proposing regulations or revising existing guidance to allow more employers to form association health plans that would be allowed to provide coverage across state lines, increase the availability of short- term, limited- duration health insurance plans, which are generally not subject to the requirements of the ACA, and increase the availability and permitted use of health reimbursement arrangements. On October 13, 2017, the Department of Justice announced that HHS was immediately stopping its cost sharing reduction payments to insurance companies based on the determination that those payments had not been appropriated by Congress. Furthermore, on December 22, 2017, former President Trump signed the Tax Cuts and Jobs Act (the " TCJA ") into law that, in addition to overhauling the federal tax system, also, effective as of January 1, 2019, repeals the penalties associated with the individual mandate. Congress or the President of the United States also could consider subsequent legislation or executive action to replace, eliminate or reaffirm elements of the ACA. We will continue to evaluate the effect that the ACA and any future measures to modify, repeal, replace or reaffirm the ACA have on our business. ~~34~~ **33** Additionally, the Inflation Reduction Act of 2022 may impact existing Medicare programs that cover prescription drugs. In addition to other relevant provisions, the Inflation Reduction Act of 2022 allow the Medicare program to directly negotiate the price of certain high- expenditure prescription drugs covered under Medicare Parts B and D, starting in the year 2028 and 2026, respectively, by setting certain" maximum fair prices." Moreover, the Inflation Reduction Act of 2022 requires manufacturers to pay rebates to the federal government if prices of certain drugs covered under the Medicare program rise faster than the rate of inflation. We will continue to evaluate the effects that the Inflation Reduction Act of 2022 will have on our business. We are not able to provide any assurance that the continued healthcare reform debate will not result in legislation, regulation, litigation or executive action by the President of the United States that is adverse to our business. Laws and other reform and cost containment measures that may be proposed and adopted in the future remain uncertain but may contain provisions that restrict our ability to price our products and / or could result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our future customers and, accordingly, our ability to generate revenue, attain profitability or commercialize our products. Risks Related to Our Reliance on Third- Parties We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans. Our drug candidate development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those drug candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or similar regulatory authorities outside the U. S., the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology (which can exist if there is a challenge to such ownership without regard to the merits of the challenge) and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our drug candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us. We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate product revenue. ~~35~~ **34** If conflicts arise between us and our collaborators or strategic partners, these parties may act in their self- interest, which may limit our ability to implement our strategies. If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in its self- interest, which may limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are

competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our drug candidates. Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts, which may adversely affect our business, results of operations and prospects. We expect to rely on third parties to conduct, supervise and monitor our clinical studies, and if these third parties perform in an unsatisfactory manner, it may harm our business. We rely on CROs, clinical investigators and clinical study sites to ensure our clinical studies are conducted properly and on time. We will have limited influence over the performance by CROs, clinical investigators and clinical study sites, and we will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. Furthermore, facilities used by these third party CROs, clinical investigators and clinical study sites may be negatively affected by catastrophic events, such as pandemics, ~~including the ongoing COVID- 19 pandemic,~~ terrorist attacks, wars or other armed conflicts, geopolitical tensions, such as the ongoing conflict between Russia and Ukraine and related sanctions and other economic disruptions or concerns, natural disasters, such as floods or fire, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third- party facility and establish a contractual relationship, which may not be readily available or on acceptable terms, which would cause additional delay and increased expense, including as a result of additional required FDA approvals, and may have a material adverse effect on our business. We, our clinical investigators, and our CROs are required to comply with the FDA' s GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we, our CROs or the clinical investigators fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and efficacy of our drug candidates. Accordingly, if our CROs or clinical investigators fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process. **35** Our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs, which must be conducted in accordance with GCPs and GLPs, respectively. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines or the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements (or for any other reasons), our clinical studies may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our pharmaceutical products. As a result, our financial results and the commercial prospects for our pharmaceutical products would be harmed, our costs could increase and our ability to generate revenues could be delayed. We may also rely on other third parties to store and distribute our products for any clinical studies that we may conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our pharmaceutical products or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue. ~~36~~ Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products. Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our products. Additionally, because our current or future collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our platforms. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a drug candidate pursuant to our agreements with our current or future collaborator would prevent us from receiving future milestone and royalty payments, which would negatively impact our revenues. If we enter into one or more collaborations, we may be required to relinquish important rights to and control over the development of our drug candidates or otherwise be subject to unfavorable terms. Any future collaborations we enter into could subject us to a number of risks, including: · We may not be able to control the amount and timing of resources that our collaborators devote to the development or commercialization of our drug candidates; · Collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new version of a drug candidate for clinical testing; · Collaborators may not pursue further development and commercialization of products resulting from the strategic partnering arrangement or may elect to discontinue research and development programs; · Collaborators may not commit adequate resources to the marketing and distribution of our drug candidates, limiting our potential revenues from these products; · Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts

management' s attention and consumes resources; · Collaborators may experience financial difficulties; · Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation; · Business combinations or significant changes in a collaborator' s business strategy may also adversely affect a collaborator' s willingness or ability to complete its obligations under any arrangement; · Collaborators could decide to move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and · Collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our drug candidates. ~~37~~ **36** We have no manufacturing, sales, marketing or distribution capabilities, and we may have to invest a significant amount of resources to develop these capabilities. We have no internal manufacturing capabilities. As a result, for manufacturing we depend on third- party manufacturers. Our strategy is based on leveraging the ability of collaboration partners to develop and manufacture our products for commercialization in the pharmaceutical marketplace, and we will be dependent on collaborations with drug development and manufacturing ~~collaborators~~ **capabilities** . If we are not able to maintain existing collaborative arrangements or establish new arrangements on commercially acceptable terms, we would be required to undertake product manufacturing and development activities at our own expense. This would increase our capital requirements or require us to limit the scope of our development activities. Moreover, we have limited or no experience in conducting full- scale bioequivalence or other clinical studies, preparing and submitting regulatory applications and distributing and marketing pharmaceutical products. As such, we are reliant on contract parties for such efforts. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. If any of our developmental collaborators breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities in a timely manner, the preclinical and / or clinical development and / or commercialization of our pharmaceutical products will be delayed and we would be required to devote additional resources to product development and commercialization or terminate certain development programs. Also, a license relationship may be terminated at the discretion of our collaborator, or at the end of contract terms, and in some cases with only limited notice to us. The termination of the collaborative arrangement could have a material adverse effect on our business, financial condition and results of operations. There also can be no assurance that disputes will not arise with respect to the ownership of rights to any technology developed with third parties. These and other possible disagreements with collaborators could lead to delays in the development or commercialization of our pharmaceutical products or could result in litigation or arbitration, which could be time- consuming and expensive and could have a material adverse effect on our business, financial condition and results of operations. Even if we decide to perform clinical trials, sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including: · We may not be able to attract clinical investigators and build effective clinical trials or a solid marketing department or sales force; · The cost of establishing an internal clinical trials program, marketing department or sales force may exceed our available financial resources and the revenue generated by any of our current product candidates, if approved, or any other pharmaceutical products that we may develop, in- license or acquire; and · Our direct sales and marketing efforts may not be successful. Any failure to perform such activities could have a material adverse effect on our business, financial condition and results of our operations. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. Because we rely on third parties to manufacture our pharmaceutical products, and because we collaborate with various organizations and academic institutions on the development of our pharmaceutical products, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. The need to share trade secrets and other confidential information when working with third parties increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business. ~~38~~ In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business. **37** Our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity. We currently have relationships with a limited number of suppliers for the manufacturing of our pharmaceutical products. Each supplier may require licenses to manufacture components if such processes are not owned by the supplier or in the public domain, and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. All entities involved in the preparation of pharmaceutical products for clinical studies or commercial sale, including our existing contract manufacturers for our drug candidates, are subject to extensive regulation. Components of a finished pharmaceutical product approved for commercial sale or used in late- stage clinical studies

must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our pharmaceutical products that may not be detectable in final product testing. Our contract manufacturers must supply all necessary documentation in support of an NDA or BLA on a timely basis and must adhere to the FDA' s GLP and cGMP regulations enforced by the FDA through its facilities inspection program. The facilities and quality systems of some or all of our third- party contractors must pass a pre- approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our pharmaceutical products or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our pharmaceutical products or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre- approval plant inspection, FDA approval of the products will not be granted. The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third- party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we, or the relevant regulatory authority, may require remedial measures that may be costly and / or time- consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon third parties with whom we contract could materially harm our business. If our third- party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a drug candidate or revocation of a pre- existing approval. As a result, our business, financial condition and results of operations may be materially harmed. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. The number of manufacturers with the necessary manufacturing capabilities is limited. In addition, an alternative manufacturer would need to be qualified through an NDA or BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines, which could materially harm our business and results of operations. ~~39~~ These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our pharmaceutical products and / or cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue, which could materially harm our business and results of operations. **38** Risks Related to Our Intellectual Property If we fail to adequately protect or enforce our intellectual property rights, we may be unable to operate effectively. Our success and ability to compete are substantially dependent on our patents, proprietary formulations and trademarks. There can be no assurance that our patents and associated trademarks and licenses will not be challenged and subsequently invalidated and / or canceled. The invalidation or cancellation of any one or all of the patents or trademarks would significantly damage our commercial prospects. Further, we may find it necessary to legally challenge parties infringing our patents or trademarks or licensed trademarks to enforce our rights thereto. There can be no assurance that any of the patents would ultimately be held valid or that efforts to defend any of the patents, trade secrets, know- how or other IP rights would be successful. The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. We own numerous U. S. and foreign patents and a number of pending patent applications that cover various aspects of our drug candidates and technologies. There can be no assurance that patents that have been issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time- consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and / or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of a product encompassed by our patents. We may have to participate in interference proceedings declared by the USPTO, which could result in a loss of the patent and / or substantial cost to us. We have filed patent applications and plan to file additional patent applications covering various aspects of our drug candidates and technologies. There can be no assurance that the patent applications for which we apply would actually be issued as patents, or do so with commercially relevant and / or broad coverage. The coverage claimed in a patent application can be significantly reduced before the patent is issued. The scope of our claim coverage can be critical to our ability to enter into licensing transactions with third parties and our right to receive royalties from our collaboration partnerships. Since publication of discoveries in scientific or patent literature often lags behind the date of such discoveries, we cannot be certain that we were the first inventor of inventions covered by our patents or patent applications. In addition, there is no guarantee that we will be the first to file a patent application directed to an invention. An adverse outcome in any judicial proceeding involving IP, including patents, could subject us to significant liabilities to third parties, require disputed rights to be licensed from or to third parties or require us to cease using the technology in dispute. In those instances where we seek an IP license from another, we may not be able to obtain the license on a commercially reasonable basis, if at all, thereby raising concerns on our ability to freely commercialize our technologies and / or products. It is also possible that we or our licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. 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 from or license to third parties. We are reliant on our licensors or licensees. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors or licensees fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. Failure to adequately protect or enforce our intellectual property rights could have a material adverse impact on our business, results of operations and prospects. ~~40~~ **39** Issued patents covering our drug candidates could be found invalid or unenforceable if challenged in court. If we or one of our licensing partners initiated legal proceedings against a third- party to enforce a patent covering one of our drug candidates, the defendant could counterclaim that the patent covering our drug candidate is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, post grant review and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our drug candidates. Such a loss of patent protection would have a material adverse impact on our business. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our 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 inventions 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 enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. 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 biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. 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. Failure to adequately protect our intellectual property rights throughout the world could have a material adverse impact on our business, results of operations and prospects. If we infringe on the intellectual property rights of others, our business and profitability may be adversely affected. Our commercial success will also depend, in part, on us and our collaborative partners not infringing on the patents or proprietary rights of others. There can be no assurance that the technologies and products used or developed by our collaborative partners and marketed and sold by us will not infringe such rights. If such infringement occurs and neither we nor our collaborative partner is able to obtain a license from the relevant third party, we will not be able to continue the development, manufacture, use or sale of any such infringing technology or product. There can be no assurance that necessary licenses to third- party technology will be available at all, or on commercially reasonable terms. In some cases, litigation or other proceedings may be necessary to defend against or assert claims of infringement or to determine the scope and validity of the proprietary rights of third parties. Any potential litigation could result in substantial costs to, and diversion of, our resources and could have a material and adverse impact on us. An adverse outcome in any such litigation or proceeding could subject us to significant liabilities, require us to cease using the subject technology or require us to license the subject technology from the third party, all of which could have a material adverse effect on our business. ~~41~~ **40** If we fail to comply with our obligations in the agreements under which we 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 are a party to a number of intellectual property license agreements that are important to our business, and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. We may need to obtain licenses from third parties to advance our research, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license

replacement technology. If we are unable to do so, we may be unable to develop the affected drug candidates, which could harm our business significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our current drug candidates or future products, resulting in either an injunction prohibiting the sales, or, with respect to the sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties. In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including: · The scope of rights granted under the license agreement and other interpretation- related issues; · The extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; · The sublicensing of patent and other rights under our collaborative development relationships; · Our diligence obligations under the license agreement and what activities satisfy those diligence obligations; · The ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and · The priority of invention of patented technology. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates, which could have a material adverse effect on our business. We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee' s former employers or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. ~~42~~ **41** We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may have in the future ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Our inability to protect our confidential information and trade secrets would harm our business and competitive position. In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position and our business. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time- consuming and unsuccessful. Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and / or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome 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. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is

a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. ~~43~~ **42** Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity and is, therefore, costly, time- consuming and inherently uncertain. In addition, the United States has enacted and is expected to continue to implement wide- ranging patent reform legislation. Further, certain U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and / or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. Provisions of the Leahy- Smith America Invents Act (the " Leahy- Smith Act "), adopted in September 2011, made a number of significant changes to U. S. patent law, the effects of which are still unfolding. The Leahy- Smith Act and its implementation, in addition to any new regulation, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and / or applications. The USPTO and various non- U. S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Non- compliance may result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, and this circumstance would have a material adverse effect on our business. ~~44~~ Risks Related to Our Business Operations **Market conditions and changing circumstances** ~~Adverse developments affecting the financial services industry~~ , ~~such as actual events~~ **some of which may be beyond** ~~or~~ **our control** ~~concerns involving liquidity~~ , ~~defaults,~~ **could impair** ~~or~~ **our** ~~non- performance by~~ **ability to access our existing cash, cash equivalents and investments and to timely pay collaborators and others. Market conditions and changing circumstances, some of which may be beyond our control, could impair our ability to access our existing cash, cash equivalents and investments and to timely pay key vendors and others. If banks and** financial institutions **with whom we have banking relationships enter receivership or become insolvent in the future, we may be unable to access, and we may lose, some or all of** ~~or~~ **our** ~~transactional counterparties~~ **existing cash** , ~~could adversely affect~~ **cash equivalents and investments to the extent** ~~the~~ **those funds are not insured or otherwise protected by the FDIC. In addition, in such circumstances we might not be able to make timely payments to our collaborators or others. The** Company **maintains** ~~' s current and projected business operations and~~ its **primary banking relationship with** ~~financial condition and results of operations. Actual events involving limited liquidity, defaults, non- performance or other adverse developments that affect financial institutions, transactional counterparties 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 March 10, 2023, Silicon Valley Bank (" SVB ") was closed by the California Department of Financial Protection and Innovation, 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 **large** ~~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 **and** ~~that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. We have substantially~~ all ~~of our~~ cash on deposit **is federally** ~~with SVB, most of which would be uninsured~~ -- **insured. The Company has** ~~by the FDIC, and we regularly maintain cash balances that are~~ not **experienced** ~~insured or are in excess of the FDIC' s insurance limit. As of March 13, 2023, we had full access to our funds. Failure to have access to our funds on deposit could have material adverse impacts on our liquidity and our current and / or projected business operations and financial condition and results of operations. Although we are not a borrower or party to~~ any ~~such instruments with SVB, Signature or any other financial institution currently in receivership, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. In this regard, counterparties to SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008- 2010 financial crisis. 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 **its accounts** the sale of such instruments , **and does not believe it** widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediate liquidity may exceed the capacity of such program. Additionally, there is **exposed** no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to **any unusual credit risk beyond** uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they **the normal credit risk currently associated with commercial** would do so in a timely fashion. Although we assess our banking relationships as we believe necessary **. However, any delay in** or **our ability to** appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or **our** capitalize **cash, cash equivalents and investments** our **or to timely pay** current and projected future business operations could be significantly impaired by factors that affect the Company, or **our collaborators and** the financial services industry or economy in general. These factors could include, among others ; events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which the Company has financial or business relationships, but could also include factors involving financial markets or the financial services industry generally. 45 The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets or the uninsured loss of deposits or other financial assets; or the termination of cash management arrangements and / or delays in accessing or actual loss of funds subject to cash management arrangements. Investor concerns regarding the U. S. or international financial 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 our customers or suppliers, which in turn, could have a material adverse effect on our current and / or projected business operations and **cause** results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us **to need to seek** , become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition **additional capital sooner** , a customer or supplier could be adversely affected by any of the liquidity or other risks that **than planned** are described above as factors that could result in material adverse impacts on the Company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution . **43** Any customer or supplier bankruptcy or insolvency, or the failure of any customer to make payments when due, or any breach or default by a customer or supplier, or the loss of any significant supplier relationships, could result in material losses to the Company and may have a material adverse impact on our business. Our future success depends on our ability to retain principal members of our executive team, consultants and advisors and to attract, retain and motivate qualified personnel. We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition **Competition** for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, consultant or advisor may impede the progress of our research and development objectives. 46 We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations. As of December 31, 2022 **2023** , we had four full- time employees. As we mature, we may need to expand our full- time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day- to- day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees, all of which may have a material adverse effect on our business, results of operations and prospects. Any future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional drug candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and / or grow revenues could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize drug candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. We are a party to collaboration agreements and other significant agreements which contain complex commercial terms that could result in disputes, litigation or indemnification liability that could adversely affect our business, results of operations and financial condition. We currently derive, and expect to derive in the foreseeable future, all or much of our revenue from collaboration agreements with biotechnology and pharmaceutical companies. These

collaboration agreements contain complex commercial terms, including: · Clinical development and commercialization obligations that are based on certain commercial reasonableness performance standards that can often be difficult to enforce if disputes arise as to adequacy of our partner' s performance; · Research and development performance and reimbursement obligations for our personnel and other resources allocated to partnered drug candidate development programs; · Clinical and commercial manufacturing agreements, some of which are priced on an actual cost basis for products supplied by us to our partners with complicated cost allocation formulas and methodologies; · Intellectual property ownership allocation between us and our partners for improvements and new inventions developed during the course of the collaboration; · Royalties on drug sales based on a number of complex variables, including net sales calculations, geography, scope of patent claim coverage, patent life, generic competitors, bundled pricing and other factors; and · Indemnity obligations for intellectual property infringement, product liability and certain other claims. From time to time, we may have informal dispute resolution discussions with third parties regarding the appropriate interpretation of the complex commercial terms contained in our agreements. One or more disputes may arise or escalate in the future regarding our collaboration agreements, transaction documents or third- party license agreements that may ultimately result in costly litigation and unfavorable interpretation of contract terms, which would have a material adverse effect on our business, financial condition and results of operations. ~~47~~ **44** We operate in an extremely competitive environment and there can be no assurances that competing technologies would not harm our business development. We are engaged in a rapidly- evolving field. Competition from numerous pharmaceutical companies is intense and expected to increase. The large and rapidly- growing market for oncology treatments is likely to attract new entrants. Numerous biotechnology and pharmaceutical companies are focused on developing cancer treatments and immuno- oncology technologies. Many, if not all, of these companies have greater financial and other resources and development capabilities than we do. Many of our competitors also have greater collective experience in undertaking preclinical and clinical testing of products, obtaining regulatory approvals and manufacturing and marketing prescription pharmaceutical products. There can be no assurance that our under- development drug candidates will be more effective or achieve greater market acceptance than competitive products or that our competitors will not succeed in developing products and technologies that are more effective than those being developed by us or that would render our products and technologies less competitive or obsolete. Additionally, there can be no assurance that the development by others of new or improved drugs will not make our pharmaceutical products superfluous or obsolete. Potential new accounting standards or legislative actions may adversely impact our future financial position or results of operations. Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses, and may affect our financial position or results of operations. New standards may occur in the future and may cause us to be required to make changes in our accounting policies. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes- Oxley Act of 2002 (or the Sarbanes- Oxley Act), new SEC regulations, Public Company Accounting Oversight Board (or PCAOB) standards and Nasdaq rules, are creating uncertainty for companies such as ours. Insurance, accounting and auditing costs are high as a result of this uncertainty and other factors. We have limited capital resources and currently have only one full- time employee in our finance department. We rely on outside consultants to supplement our internal expertise and are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue- generating activities to compliance activities. Risks Related to Our Common Stock ~~Our failure~~ **We may not continue** to meet the continued listing requirements of ~~The~~ Nasdaq ~~Capital Market~~ **, which** could result in a ~~de-~~ **delisting of our common shares. Our common shares are listed on the Nasdaq. While we are currently in compliance, we have in the past been, and may in the future be, unable to comply with certain** listing **standards that we are required to meet to maintain the listing** of our common **shares on the** ~~stock. Failure to regain compliance with~~ Nasdaq ~~listing rules could affect the market price of our Common Stock and liquidity and reduce our ability to raise capital~~ . ~~Currently~~ **For instance** , ~~our Common Stock trades~~ on ~~the Nasdaq Capital Market. On~~ June 3, 2022, we received ~~a~~ written notification ~~(the " Notice ")~~ from the Listing Qualifications Department of ~~the NASDAQ Stock Market LLC (" Nasdaq ")~~ notifying us that the closing bid price for our common stock had been below $ 1. 00 for 30 consecutive business days and that we **,** therefore **,** were not in compliance with the **Nasdaq** minimum bid price requirement ~~for continued inclusion on The Nasdaq Capital Market under Nasdaq Listing Rule 5550 (a) (2) (the " Bid Price Requirement ")~~ . **After approval from** ~~The Notice has no immediate effect on the listing of~~ the Company' s **Board of Directors, on May 15, 2023, we effected a reduction, on a 1- for- 10 basis, in our authorized** common stock ~~on the Nasdaq Capital Market. Under the Nasdaq Listing Rules~~ , **par value $ 0. 001, along** ~~we had a period of 180 calendar days from the date of the Notice to regain compliance~~ with **a corresponding and proportional decrease in** the ~~Bid Price Requirement~~ **number of shares issued and outstanding (the " Reverse Stock Split ")** . **On May** ~~Accordingly, we had until November~~ 30, ~~2022~~ **2023** ~~(the" Compliance Date"), to regain compliance with the Bid Price Requirement. On December 1, 2022~~ , we received a letter from Nasdaq ~~informing~~ **notifying** us that **we** ~~although the Company' s common stock~~ had ~~not~~ regained compliance with the minimum ~~$ 1. 00 bid price per share requirement, Nasdaq had determined that we were eligible for an additional 180 calendar day period, or until May 29, 2023, to regain compliance. Nasdaq' s determination was based on the Company meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of the~~ bid price requirement **as** ~~, and our written notice of its intention to cure the deficiency during the second compliance period by effecting~~ a **result of** ~~reverse stock split, if necessary. 48 If at any time before May 29, 2023,~~ the closing bid price of our common stock ~~closes~~ **being** at ~~or above~~ $ 1. 00 per share **or greater** for **the** ~~a minimum of, subject to Nasdaq' s discretion,~~ 10 consecutive business days **from May 15** , ~~Nasdaq~~ **2023 through May 26, 2023 and that this matter was closed. The primary intent for the Reverse Stock Split was that the anticipated increase in the price of our common shares immediately following and**

resulting from a reverse stock split due to the reduction in the number of issued and outstanding common shares would help us meet the minimum bid price requirement. It cannot be assured that the Reverse Stock Split will ~~provide written notification that~~ **result in any sustained proportionate increase in the market price of our common shares, which is dependent upon many factors, including the business and financial performance of the company, general market conditions, and prospects for future success, which are unrelated to the number of shares of our common shares outstanding. It is not uncommon for the market price of a company' s common shares to decline in the period following a reverse stock split. Thus, while** we have ~~achieved~~ **regained** compliance with the ~~Bid Price Requirement. We will continue~~ **continued listing** ~~to monitor the closing bid price of our common stock and will consider our available options to resolve the deficiency and regain compliance with the Bid Price Requirement~~ **requirements for Nasdaq** ~~within the allotted compliance period. However~~ , ~~there can~~ **it cannot** be ~~no assurance~~ --- **assured** that we will **continue** ~~be able~~ to **do so. If** ~~regain compliance with the Bid Price Requirement, or will otherwise be in compliance with other~~ Nasdaq **delists our common shares from trading on its exchange for failure to meet the** ~~Listing~~ **listing standards** ~~Rules. If we fail to regain compliance with the Nasdaq Listing Rules~~ , ~~including the Bid Price Requirement~~ **an investor would likely find it significantly more difficult to dispose of or obtain our shares** , ~~we~~ **and our ability raise future capital through the sale of our shares** could be ~~delisted and our stock~~ **severely limited. Delisting** ~~would~~ **could also have** ~~be considered a penny stock under regulations of the~~ **other** ~~SEC~~ **negative results** , **including the potential loss of confidence by employees, the loss of institutional investor interest** and **fewer business development opportunities** ~~would therefore be subject to rules that impose additional sales practice requirements on broker- dealers who sell our securities~~ . **45** The **Reverse Stock Split may decrease** ~~additional burdens imposed upon broker- dealers by these~~ -- **the liquidity of our common shares. The liquidity of** ~~requirements could discourage broker-dealers from effecting transactions in~~ our common stock ~~, which could severely limit~~ **may be adversely affected by** the ~~market liquidity~~ **reduced number of shares outstanding after the Reverse Stock Split. In addition, the Reverse Stock Split may have increased the number of shareholders who own odd lots (less than 100 shares)** of our common **shares** ~~stock and stockholder' s ability to sell our securities in the secondary market. If our common stock were to be delisted from the NASDAQ Capital Market~~ , **creating** the **potential** ~~liquidity of our common stock would be materially affected, which would decrease the attractiveness of our common stock to investors and result in a decline in the market price of our common stock. Also, it may be difficult~~ for ~~us~~ **such shareholders** to ~~raise additional capital if we are not listed on a major exchange~~ **experience an increase in the cost of selling their shares and greater difficulty effecting such sales** . The market price of our securities may be highly volatile, and you may not be able to sell our securities. Companies trading in the stock market in general have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our securities, regardless of our actual operating performance. The market price of our securities may be volatile. Our securities could be subject to wide fluctuations in price in response to a variety of factors, including the following: **· Failure to realize the anticipated potential of the DNase or PolyXen technologies;** · Adverse results, delays, or holds in pre- clinical or clinical studies; · Inability to obtain additional funding; · Any delay in filing an IND or BLA for any of our drug candidates and any adverse development or perceived adverse development with respect to the FDA' s review of that IND or BLA; · Failure to develop successfully our drug candidates; · Failure to maintain our existing strategic collaborations or enter into new collaborations; · Failure by us or our licensors and strategic collaboration partners to prosecute, maintain or enforce our intellectual property rights; · Changes in laws or regulations applicable to future products; · Inability to obtain adequate product supply for our drug candidates or the inability to do so at acceptable prices; · Adverse regulatory decisions; · Introduction of new products, services or technologies by our competitors; · Failure to meet or exceed financial projections we may provide to the public; · Failure to meet or exceed the financial projections of the investment community; · The perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community; · Announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partner or our competitors; · Disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; · Additions or departures of key scientific or management personnel; · Significant lawsuits, including patent or stockholder litigation; · Changes in the market valuations of similar companies; · Sales of our securities by us or our stockholders in the future; · Adverse economic conditions, including potential adverse effects of public health issues, such as the coronavirus outbreak, and geopolitical events, such as the Russian invasion of Ukraine, and related sanctions and other economic disruptions or concerns, on economic activity generally; and · Trading volume of our securities. ~~49~~ **46** Our preferred ~~stock has~~ **stockholders have** rights, preferences and privileges that are not held by, and are preferential to, the rights of our common stockholders, which could result in the interests of ~~the holders of~~ our preferred ~~stock~~ **stockholders** differing from those of our common stockholders. The holders of our preferred stock have the right to receive a liquidation preference entitling them to be paid out of our assets available for distribution to stockholders before any payment may be made to holders of any common stock or any series of preferred stock ranked junior to such class of preferred stock. The existence of a liquidation preference may reduce the value of our common stock, make it harder for us to sell shares of common stock in offerings in the future or prevent or delay a change of control. Additionally, each share of ~~Series A Preferred Stock and~~ Series B Preferred Stock are convertible into shares of our common stock, subject to an issuable maximum and subject to certain adjustments, which may cause significant dilution to our common stockholders. The preferential rights could result in divergent interests between the holders of shares of preferred stock and holders of our common stock. The issuance of future shares of common stock may result in dilution to our stockholders. As of March ~~10~~ **15** , 2023, we had approximately ~~15~~ **1** . ~~2~~ **5** million shares of common stock outstanding, excluding ~~6~~ **0** . ~~8~~ **7** million of potentially dilutive common stock related to outstanding preferred stock, warrants, options, restricted stock and common stock awards. The issuance of these shares of common stock and the sale of these shares of common stock, or even the potential of such issuance and sale, may have a depressive effect on the market price of our common

stock, and the issuance of such common stock will cause dilution to our stockholders. We could be subject to securities class action litigation. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because **we** ~~pharmaceutical companies~~ have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. An active, liquid and orderly market for our common stock or purchase warrants may not develop. Our common stock and purchase warrants trade on **the** Nasdaq **Capital Market** . An active **, liquid** trading market for our common stock or purchase warrants may never develop or be sustained. If an active **, liquid** market for our common stock or purchase warrants does not continue to develop or is not sustained, it may be difficult for investors to sell shares or purchase warrants without depressing the market price, and investors may not be able to sell the shares or purchase warrants at all. An inactive **or illiquid** market may also impair our ability to raise capital by selling common stock or purchase warrants and may impair our ability to acquire other businesses, applications or technologies using our common stock or purchase warrants as consideration, which, in turn, could materially adversely affect our business. We have entered into several agreements with our stockholders. We have in the past, and may continue to enter into from time to time, agreements with our stockholders, which may result in conflicts of interest. In addition, these arrangements may not have been negotiated at arm' s length and may contain terms and conditions that are not in our best interest. ~~50~~ **Actions of activist shareholders could cause us to incur substantial costs, divert management' s attention and resources, and have an adverse effect on our business. We actively engage in discussions with our shareholders regarding further strengthening our Company and creating long- term shareholder value. Some shareholder activism, including potential proxy contests, could result in substantial costs, such as legal fees and expenses, disrupt our operations, and divert management' s and our Board of Directors' attention and resources from our business and strategic plans. Public shareholder activism can create perceived uncertainties as to our future direction, strategy, or leadership and may result in the loss of potential business opportunities, harm our ability to attract new employees, investors, collaborators and other partners, and cause our stock price to experience volatility. These risks could adversely affect our financial performance. 47** We do not intend to pay dividends on our common stock or preferred stock so any returns will be limited to the value of our stock. We have never declared or paid any cash dividends on our common stock or preferred stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to common or preferred stockholders will therefore be limited to the appreciation of their stock. Certain provisions of our Articles of Incorporation, Bylaws, and the Nevada Revised States may be deemed to have an anti- takeover effect, which could cause the market price of our common stock to decline. Certain provisions of our Articles of Incorporation, Bylaws, and the Nevada Revised States may be deemed to have an anti- takeover effect. Such provisions may delay, deter or prevent a tender offer or takeover attempt that a stockholder might consider to be in that stockholder' s best interests, including attempts that might result in a premium over the market price for the shares held by stockholders, which could cause the market price of our common stock to decline. General Risk Factors Our financial condition, results of operations, business and cash flow may be negatively affected by unfavorable U. S. or global economic conditions. Our financial condition, results of operations, business and cash flow may be negatively affected by general conditions in the global economy and in the global financial markets and uncertainty about economic stability. The global economy has experienced extreme volatility and disruptions, including as a result of public health epidemics and pandemics, or other outbreaks of communicable diseases, such as the COVID- 19 pandemic, as well as from international conflicts, terrorism or other geopolitical events, such as the Russian invasion of Ukraine, and related sanctions and other economic disruptions or concerns. ~~For example, the global pandemic related to the rapidly growing outbreak of a novel strain of coronavirus (COVID- 19) has created, and may continue to create, significant volatility, uncertainty and economic disruption, including significant volatility in the capital markets. The extent to which the COVID- 19 pandemic affects our business, operations, financial results and the trading price of our common stock will depend on numerous evolving factors that we may not be able to accurately predict. If the global response to contain the COVID- 19 pandemic escalates further or is unsuccessful, or if governmental decisions to ease pandemic related restrictions are ineffective, premature or counterproductive, we could experience a material adverse effect on our business, financial condition, results of operations and cash flows.~~ Additionally, the global economy and financial markets may also be adversely affected by the current or anticipated impact of military conflict, terrorism or other geopolitical events **, such as the wars in Ukraine and the Middle East** . Sanctions imposed by the United States and other countries in response to such conflicts, may also adversely impact the financial markets and the global economy, and the economic countermeasures by the affected countries or others could exacerbate market and economic instability. **For example** ~~In late February 2022~~ , **in response to the** ~~Russia~~ **Russian invasion of** ~~initiated significant military action against~~ Ukraine ~~. In response~~ , the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions ~~if~~ **as** the conflict continues or **if it** worsens. It is not possible to predict the broader consequences of ~~the~~ **such** conflict **or any others, such as the war in the Middle East** , including related geo- political tensions, and the measures and retaliatory actions that will be taken by the United States and other countries in respect thereof, as well as any countermeasures or retaliatory actions Russia **or any other country** may take in response, are likely to cause regional instability and geo- political shifts and could materially adversely affect global trade, currency exchange rates, regional economies, and the global economy. While it is difficult to anticipate the impact of any of the foregoing on our Company in particular, the conflict and actions taken in response to the conflict could increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations. ~~51~~ There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for any product candidates we

may develop and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could impair our ability to achieve our growth strategy, could harm our financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that our current or future service providers, manufacturers or other collaborators may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. We cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. **48** Our ability to use potential future operating losses and our federal and state NOL carryforwards to offset taxable income from revenue generated from operations or corporate collaborations could be limited. The use of our NOL carryforwards may have limitations resulting from certain future ownership changes or other factors under the Code and other taxing authorities **, including foreign tax regimes** . The TCJA changed both the federal deferred tax value of the NOL carryforwards and the rules of utilization of federal NOL carryforwards. If our NOL carryforwards are limited, and we have taxable income which exceeds the available NOL carryforwards for that period, we would incur an income tax liability even though NOL carryforwards may be available in future years prior to their expiration. Any such income tax liability may adversely affect our future cash flow, financial position and financial results. Tax reform may significantly affect the Company and our stockholders. Due to the potential for changes to tax laws and regulations or changes to the interpretation thereof, the ambiguity of tax laws and regulations, the subjectivity of factual interpretations and other factors, our estimates of effective tax rate and income tax assets and liabilities may be incorrect and our financial statements could be adversely affected. The impact of these factors referenced in the first sentence of this paragraph may be substantially different from period- to- period. In addition, the amount of income taxes we pay is subject to ongoing audits by U. S. federal, state and local tax authorities and by non- U. S. tax authorities. If audits result in payments or assessments different from our reserves, our future results may include unfavorable adjustments to our tax liabilities and our financial statements could be adversely affected. Any further significant changes to the tax system in the United States or in other jurisdictions (including changes in the taxation of international income as further described below) could adversely affect our financial statements. Governments may impose price controls, which may adversely affect our future profitability. We intend to seek approval to market our drug candidates in both the United States and in foreign jurisdictions. In some foreign countries and jurisdictions, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials to compare the cost effectiveness of our drug candidates to other available therapies, which is time- consuming and costly. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability. ~~52~~ Our employees, principal investigators, consultants and commercial partners 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 of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non- U. S. regulators, provide accurate information to the FDA and non- U. S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. 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. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation or could cause regulatory agencies not to approve our drug candidates. It is not always possible to identify and deter employee misconduct, 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. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. **49** Use of our drug candidates could be associated with adverse side effects. As with most biopharmaceutical products, use of our drug candidates could be associated with side effects or adverse events which can vary in severity and frequency. Side effects or adverse events associated with the use of our drug candidates may be observed at any time, including in clinical trials or once a product is commercialized, and any such side effects or adverse events may negatively affect our ability to obtain regulatory approval or market our drug candidates. Side effects such as toxicity or other safety issues associated with the use of our drug candidates could require us to perform additional studies or halt development or sale of these drug candidates or expose us to product liability lawsuits which will harm our business. The emergence of unforeseen safety issues or adverse events may lead to regulatory agencies requiring us to conduct additional preclinical or clinical trials regarding the safety and efficacy of our drug candidates, which we have not planned or anticipated. We cannot assure you that we will resolve any issues related to any product- related adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or ever, which could harm our business, prospects and financial condition. We may also inadvertently fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or other foreign regulatory agencies could take action including criminal prosecution, the imposition of civil monetary penalties, seizure of our products, or delay in approval or clearance of

future products. ~~53~~ We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our drug candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our drug candidates, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims. The use of our drug candidates in clinical studies and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our drug candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in **, among other negative effects** : · Impairment of our business reputation; · Withdrawal of clinical study participants; · Costs due to related litigation; · Distraction of management' s attention from our primary business; · Substantial monetary awards to patients or other claimants; · The inability to commercialize our drug candidates; and · Decreased demand for our drug candidates, if approved for commercial sale, all of which may have a material adverse effect on our business, results of operations and prospects. 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 third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. **50** The workers' compensation insurance we maintain to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work- related injuries may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which may have a material adverse effect on our business and results of operations. Non- cash charges such as share- based payments may adversely impact our results of operations. We record non- cash charges related to share- based expense, which could fluctuate materially as the Company expects to continue to issue share- based payments awards and may adversely impact our results of operations. ~~54~~ Varying interpretations of existing **accounting** standards and rules have occurred with frequency and may cause us to have to restate previously reported result of operations. Varying interpretations of existing standards of accounting policies or accounting treatments of existing transactions may cause us to have to restate previously reported result of operations. 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. 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, which may have a material adverse effect on our business and results of operations. Failure in our information technology systems **or those of our third- party service providers** , including by cybersecurity attacks or other data security incidents, could significantly disrupt our operations. Our operations depend, in part, on the continued performance of our information technology systems **, which are cloud- based and maintained by third- party service providers** . Our information technology systems are potentially vulnerable to physical or electronic break- ins, computer viruses and similar disruptions. Failure of our information technology systems could adversely affect our business, profitability and financial condition. A successful cybersecurity attack or other data security incident could result in the misappropriation and / or loss of confidential or personal information, create system interruptions or deploy malicious software that attacks our systems. It is possible that a cybersecurity attack might not be noticed for some period of time. The occurrence of a cybersecurity attack or incident could result in business interruptions from the disruption of our information technology systems, or negative publicity resulting in reputational damage with our clinical trial participants, customers, stockholders and other stakeholders and / or increased costs to prevent, respond to or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business. **51** We are a smaller reporting company, and the reduced reporting requirements applicable to smaller reporting companies may make our common stock less attractive to investors. We are a smaller reporting company (" SRC "), which allows us to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not SRCs, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act of 2002, as amended, reduced disclosure obligations regarding executive compensation in our Annual Report and our periodic reports and proxy statements and providing only two years of audited financial statements in our Annual Report and our periodic reports. We will remain an SRC until (a) the aggregate market value of our outstanding common stock held by non- affiliates as of the last business day our most recently completed second fiscal quarter exceeds $ 250 million or (b) (1) we have over $ 100 million in annual revenues and (2) the aggregate market value of our outstanding common stock held by non- affiliates as of the last business day our most recently completed second fiscal quarter exceeds $ 700 million. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some

investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile and may decline.