Risk Factors Comparison 2025-04-15 to 2024-03-06 Form: 10-K

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An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks described below, together with other information appearing elsewhere in this Annual Report, including our financial statements and the related notes and the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock. Risk Factor Summary The following is a summary of the risk factors included in this Item 1A and is qualified entirely by the disclosure included in the rest of this Item 1A: Risks Related to Our Financial Position and Capital Needs ● • We have incurred and expect to continue to incur substantial operating losses and our ability to use our net operating losses to offset future taxable income may be subject to certain limitations. ● **The report of our independent registered public accounting firm included a " going concern " explanatory paragraph. We identified a material weakness in our internal control over financial reporting as of December 31, 2024 and this or other material weaknesses could continue to materially impair our ability to report accurate financial information in a timely manner.** Our operating history makes evaluating our business and future viability more difficult. ● We **need** ~~will require~~ substantial ~~additional~~ funding to **operate** ~~finance our operations~~, and **failure** ~~may suffer consequences~~ to **secure it may harm** our development programs ~~upon failure to do so~~. ● Raising additional capital may cause adverse effects. Risks Related to the Development and Commercialization of Our Product Candidates ● **The Warning Letter from FDA could impede our current and future clinical trials or NDA submissions.** Our success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates and may be adversely affected upon failure to do so. ● **We received the Complete Response Letter from the FDA indicating that our new drug application or NDA for govorestat for the treatment of Classic Galactosemia was not approvable at this time, and do not know if govorestat or any of our product candidates will ever receive regulatory approval.** We or Advanz Pharma may fail to perform under **our partnership** ~~any of the~~ agreements ~~entered into in connection with the partnership~~ for ~~the commercialization of~~ AT- 007 **(govorestat) commercialization** , **potentially leading** ~~which may subject us~~ to liabilities ~~,~~ and ~~we may fail to achieve~~ **unachieved** ~~anticipated~~ benefits ~~of the partnership~~. ● Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and our results may not be sufficient for the necessary regulatory approvals. ● Clinical drug development involves a lengthy and expensive process and the development of additional product candidates is risky and uncertain. ● We may be unable to obtain ~~/~~ **or** maintain ~~or receive the benefits of~~ regulatory ~~approval~~ **approvals** , ~~rare pediatric disease designation~~ **designations** ~~/ exclusivity~~, **or** accelerated ~~registration~~ pathways ~~, breakthrough therapy designations or fast track designations~~ for our product candidates ~~, as applicable~~. ● Clinical trials are expensive, time consuming and subject to factors outside our control. ● Our product candidates may cause undesirable side effects, affecting regulatory approval, commercial potential or result in significant negative consequences following any potential marketing approval. ● • Interim, " top ~~-~~ line " and preliminary data from our clinical trials may be subject to change. • ~~● The market~~ **Market** opportunities for our ~~product~~ **products** ~~candidates~~ may be smaller ~~than we believe~~ or approval ~~we obtain~~ may narrow our patient population. ● • We may face substantial competition. ● • We may face risks related to strategic collaborations to develop our product candidates ~~● Our~~ • **We may experience sudden changes in the regulatory standards that govern the acceptability of our clinical studies to support approval. • Even if approved, our** ~~product~~ **products** ~~candidates~~ may **not** ~~fail to~~ achieve market acceptance necessary for commercial success. ● • We may face risks **from** ~~related to any~~ potential international operations **if we commercialize any product candidate** . ● • We may be adversely affected by product liability lawsuits. ● • Our insurance policies may be inadequate and potentially expose us to unrecoverable risks. Risks Related to Regulatory Compliance ● • We are subject to healthcare laws and regulations, which **are subject to change and** carry substantial penalties for noncompliance. ● • Coverage and adequate reimbursement may not be available for our product candidates. ● • Healthcare reform measures may have a negative impact on our business and results of operations. Risks Related to Our Dependence on Third Parties ● • **One of our clinical investigators received a warning letter from the FDA following a site inspection.** • Third- parties may conduct our preclinical studies and clinical trials in an unsatisfactory manner. ● • We intend to rely on third parties to produce supplies of our product candidates. ● • We and our third- party affiliates are subject to environmental, health and safety laws and regulations. Risks Related to Our Intellectual Property ● • Breaches of our license agreements may result in the adverse effects to our ability to continue the development and commercialization of our product candidates. ● • Insufficient patent protection could **let** ~~allow our~~ competitors ~~to~~ develop **similar** ~~and commercialize~~ products ~~and technology similar or identical to ours~~. ● • Obtaining and maintaining our patent rights is expensive, complicated and labor intensive and patent terms may be inadequate to protect our competitive position on our product candidates. ● • We may be subject to claims alleging violations of intellectual property rights. ● • Changes in patent law could impair our ability to protect our product candidates. ● • We may be unable to protect our intellectual property rights. ● • Intellectual property rights do not necessarily address all potential threats to our business. Risks Related to Our Business Operations, Employee Matters and Managing Growth ● • We ~~are highly dependent on the services of~~ **face securities- related class- action and shareholder derivative litigation that could be costly, divert resources, and damage our reputation, business,** ~~our~~ **or** ~~current executive~~

~~officers~~ **financial condition if an adverse judgment occurs** . ~~•~~ **• Recent leadership changes, including our founder and CEO' s departure, may cause uncertainty. •** We may experience difficulties resulting from the expansion of our organization. ~~•~~ • We may be subject to security breaches in our information technology systems. ~~•~~ • Our employees and the third- parties we deal with may engage in misconduct or improper activities. ~~• Our business may be adversely affected by the coronavirus outbreak.~~ Risks Related to Ownership of Our Common Stock ~~•~~ • The market price of our common stock is volatile ~~and ,~~ has fluctuated substantially **and significantly declined** . ~~• Concentration~~ **• Failure to regain compliance with the continued listing requirements** of ~~ownership of~~ **Nasdaq could result in** our common stock **being delisted** ~~among our existing executive officers, directors~~ and **the price of our common stock could be negatively impacted** ~~principal stockholders may prevent new investors from influencing significant corporate decisions~~ . ~~•~~ • We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. General Risk Factors ~~•~~ • We may be affected by unfavorable research or reports. ~~•~~ • We may use our cash and cash equivalents ineffectively or in ways with which you do not agree. ~~•~~ • We **face** ~~are subject to~~ risks ~~as an~~ **and costs from losing** " emerging growth company " **status** and ~~a public company~~ **must meet new requirements** . ~~•~~ • We may **use** ~~avail ourselves of~~ defensive and forum selection provisions in our governing documents and ~~under~~ Delaware law. ~~41Risks~~ -- **Risks** Related to Our Financial Position and Capital NeedsWe have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability. Since inception in January 2016, we have incurred significant operating losses. Our net loss was $ **105. 6 million and $** 119. 8 ~~million and $ 82. 5~~ million for the years ended December 31, **2024, and** 2023 ~~, and 2022~~ respectively. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~468~~ **574** . ~~6~~ **2** million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. To date, we have never obtained regulatory approval for, or commercialized, any drugs. It could be several years, if ever, before we have a commercialized drug. The net losses we incur may fluctuate significantly from quarter to quarter and year- to- year. We anticipate that our expenses will increase substantially if, and as, we: ~~•~~ • continue the ongoing and planned development of our product candidates; ~~•~~ • initiate, conduct and complete any ongoing, anticipated or future preclinical studies and clinical trials for our current and future product candidates; ~~•~~ • seek marketing approvals for any product candidates that successfully complete clinical trials; ~~•~~ • establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any current or future product candidate for which we may obtain marketing approval; ~~•~~ • seek to discover and develop additional product candidates; ~~•~~ • continue to build a portfolio of product candidates through the acquisition or in- license of drugs, product candidates or technologies; ~~•~~ • maintain, protect and expand our intellectual property portfolio; ~~•~~ • meet the requirements and demands of being a public company; ~~•~~ • defend against any product liability claims or other lawsuits related to our products; ~~•~~ • hire additional **executive,** clinical, regulatory and scientific personnel; and ~~•~~ • add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts. Furthermore, we have **recently** incurred **and likely will continue to incur** additional costs associated with ~~operating as a public company~~ **the Complete Response Letter we received from the FDA in November 2024 for the new drug application (NDA) we submitted for govorestat for the treatment of Classic Galactosemia, the Warning Letter related to the Phase 2 / 3, ACTION- Galactosemia Kids study, the departure of our founder and CEO and securities- related class action litigation and derivative litigation** , including significant legal, accounting, investor relations and other expenses. To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our current and future product candidates, obtaining regulatory approval, procuring commercial- scale manufacturing, marketing and selling any products for which we obtain regulatory approval (including through third parties), as well as discovering or acquiring and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are sufficient to offset our expenses and achieve profitability. Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any **additional** delays in the initiation and completion of our clinical trials or the development **and approval** of any of our product candidates, our expenses ~~could~~ **will likely** increase. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. ~~A~~ **Any additional** decline in the value of our common stock could also cause you to lose all or part of your investment. **The report of our independent registered public accounting firm included a " going concern " explanatory paragraph. The report of our independent registered public accounting firm on our financial statements for the year ended December 31, 2024 includes an explanatory paragraph regarding the existence of substantial doubt about our ability to continue as a going concern.** ~~42Our~~ -- **Our cash and cash equivalents were $ 79. 4 million at December 31, 2024. We will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities. Additionally, we may encounter unforeseen expenses, including in connection with reevaluating our product candidates and potential new trials. Given our planned expenditures for the next several years, we have concluded, and our independent registered public accounting firm has agreed with our conclusion that there is still a substantial doubt regarding our ability to continue as a going concern for a period of 12 months beyond the filing of this Annual Report on Form 10- K. Any such inability to continue as a going concern may result in our stockholders losing their entire investment. There is no guarantee that we will become profitable or secure**

additional financing on acceptable terms. We identified a material weakness in our internal control over financial reporting as of December 31, 2024 and this or other material weaknesses could continue to materially impair our ability to report accurate financial information in a timely manner. Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of its disclosure controls and procedures as defined in Rules 13a- 15 (e) and 15d- 15 (e) under the Exchange Act for the year ended December 31, 2024. Based on such evaluation, the principal executive officer and principal financial officer has concluded that our disclosure controls and procedures were not effective as of December 31, 2023 due to the identified material weakness in internal control over financial reporting as discussed below. Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a- 15 (f) and 15d- 15 (f) of the Exchange Act). Our management, under the supervision and with the participation of the principal executive officer and principal financial officer, conducted an assessment of the effectiveness of internal control over financial reporting as of December 31, 2024, based on the framework and criteria established in Internal Control- Integrated Framework (2013) (the " COSO framework ") issued by the Committee of Sponsoring Organizations of the Treadway Commission (" COSO "). Based on this assessment, management concluded that, as of December 31, 2023, its internal control over financial reporting was not effective due to the existence of the material weakness described below. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that a reasonable possibility exists that a material misstatement of the annual or interim financial statements would not be prevented or detected on a timely basis. Our management identified a deficiency in our internal control over financial reporting that gave rise to a material weakness. The deficiency primarily related to deficiencies in the principles associated with the information and communication component of the COSO framework. This material weakness resulted in not having effective communication process to ensure that relevant and reliable information was communicated timely across the organization to enable management to effectively carry out their financial reporting and internal control roles and responsibilities. As further described in Item 9A below, our management has been engaged in developing and implementing a remediation plan to address the material weakness described above. However, the material weakness will not be fully remediated until management can demonstrate the full effectiveness of controls over a sufficient period of time, and we can give no assurance on the success of such measures or the outcome of our assessment of these measures at this time. If the steps we take to remediate the material weakness are ineffective, the material weakness could result in material misstatements to our annual or interim consolidated financial statements that might not be prevented or detected on a timely basis, or in delayed filings of our required periodic reports. This might lead to investors losing confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be adversely affected, and we could become subject to litigation or investigations by Nasdaq, the SEC or other regulatory authorities, which could require additional financial and management resources. Furthermore, if we identify any new material weaknesses in the future, any such newly identified material weakness could limit our ability to prevent or detect a misstatement of our accounts or disclosures that could result in a material misstatement of our annual or interim financial statements. In such case, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We cannot assure you that the measures we have taken to date, or any measures we may take in the future, will be sufficient to remediate our existing material weakness or avoid potential future material weaknesses. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which would adversely affect investor confidence in our company and harm our business. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations in a timely manner, or at all. Testing by us conducted in connection with Section 404 (a) of the Sarbanes Oxley Act may reveal material weaknesses in our internal controls over financial reporting related to our limited finance, accounting and IT staffing levels. For example, in connection with the audit of our financial statements for the year ended December 31, 2023, we identified a material weakness in our internal control over financial reporting related to deficiencies in our controls over the financial statement close process, which was fully remediated as of March 31, 2024. In addition, as further described in Item 9A below, in connection with the audit of our financial statements for the year ended December 31, 2024, we identified a material weakness related to deficiencies in the principles associated with the information and communication component of the COSO framework. While we are implementing our remediation plan, we cannot provide assurances that the measures that have been taken to date, and are continuing to be implemented, will be sufficient to remediate the material weakness identified or to avoid potential future materials weaknesses. Subsequent testing by our independent registered public accounting firm in connection with Section 404 (b) of the Sarbanes Oxley Act may reveal continued or additional deficiencies in our internal controls over financial reporting that are deemed to be significant deficiencies or material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Ineffective internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. We are required to disclose material changes made in our internal controls over financing reporting and procedures on a quarterly basis and our management are required to assess the effectiveness of these controls annually. We are also required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be a non- accelerated filer, we will be required to

include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, for as long as we are a smaller reporting company under the JOBS Act or a non- accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404 (b) of the Sarbanes- Oxley Act. To achieve compliance with Section 404 (a) of the Sarbanes- Oxley Act, we engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to implement our remediation plan, continue to dedicate internal resources, potentially engage additional outside consultants to assess the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively and implement a continuous reporting and improvement process for internal control over financial reporting. We determined that, as of December 31, 2024, our disclosure controls and procedures were not effective due to the identified material weakness in internal control and financial reporting as described herein. The effectiveness of our internal controls in future periods is subject to the risk that our controls may become further inadequate because of changes in conditions. We may be unable to timely remediate our material weakness and may discover additional weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system' s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities including equivalent foreign authorities. Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. We are a clinical- stage company with limited operational history, and our operations to date have been largely focused on raising capital, organizing and staffing our company, identifying and developing our product candidates, and undertaking preclinical and clinical development for our product candidates. As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial- scale product or conduct sales and marketing activities necessary for successful commercialization, or arrange for a third- party to conduct these activities on our behalf. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history. ~~We have encountered~~ **In connection with our efforts to address the issues referenced in the Warning Letter** , **including reevaluating govorestat for the treatment of Classic Galactosemia** and ~~may continue~~ **Sorbitol Dehydrogenase SORD Deficiency, we expect** to encounter **significant additional expenses, including expenses that we had not expected, as well as additional** unforeseen expenses, difficulties, complications, delays **,** and other known or unknown factors in achieving our business objectives. ~~We~~ **If we are successful in our clinical trials for a product candidate, we** will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. Additionally, we expect our financial condition ~~and operating results~~ to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate certain of our development programs or other operations. As of December 31, ~~2023~~ **2024** , we had $ ~~49~~ **79** . ~~9~~ **4** million in cash and cash equivalents. ~~After giving effect to our issuance of shares of common stock under the Leerink ATM Agreement in January and February 2024, which resulted in net proceeds of $ 12. 5 million (after deducting placement agent commissions and other offering expenses), the exercise of our Common Warrants in January and February 2024, which resulted in net proceeds of $ 4. 0 million, and the March 1, 2024 completion of our sale of a total of 12, 285, 714 shares of common stock, at a purchase price of $ 7. 00 per share, and 2, 000, 000 Pre- Funded Warrants, at a purchase price of $ 6. 9999 per Pre Funded Warrant, in a private placement (the " March 2024 Private Placement "), which resulted in net proceeds of approximately $ 100 million (before deducting placement agent commissions and other offering expenses), we have $ 153. 5 million in cash and cash equivalents as of March 1, 2024.~~ We ~~believe that our cash and cash equivalents as of December 31, 2023, along with proceeds from the ATM, exercise of our Common Warrants in January and February 2024, the completion of the March 2024 Private Placement and with the projected clinical and regulatory milestone payments expected in fiscal year 2024 from Advanz Pharma will be sufficient to fund our operations into 2026, and potentially beyond if drug approvals materialize in the expected timelines. However, we~~ will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities **. Additionally, we may encounter unforeseen expenses, including in connection with reevaluating our product candidates and potential new trials. There is no assurance that we will be able to obtain such additional financing on favorable terms or at all, or to fund our operations beyond that point** . Our future capital requirements will depend on many factors, including: ~~•~~ • the timing, progress and results of our ongoing preclinical studies and clinical trials of our product candidates; ~~•~~ • **FDA requirements for the approval of govorestat for any indication; •** the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of other product candidates that we may pursue; ~~•~~ • our ability to establish collaborations on favorable terms, if at all; ~~•~~ • the costs, timing and outcome of regulatory review of our product candidates; ~~•~~ • the costs and timing of future commercialization activities **if we are successful in reaching commercialization of any product**

candidate , including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval; ~~•~~ • the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval **, if any** ; ~~•~~ • the cost of any milestone and royalty payments with respect to any approved product candidates; ~~•~~ • the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims; ~~• 43 •~~ the costs of operating as a public company; and ~~•~~ • the extent to which we acquire or in- license other product candidates and technologies. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. We may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. In addition, our ability to access additional capital has ~~been~~ **and will be** affected by **the decrease in our common stock trading price and the Complete Response Letter for the govorestat NDA for Classic Galactosemia and the Warning Letter we received from the FDA which may have damaged our reputation, as well as** overall macroeconomic trends ~~, among other things, including rising interest rates,~~ which have caused the price of our common stock to fluctuate significantly and / or decline **significantly** . ~~These macroeconomic trends have been exacerbated by recent hostilities between Russia and Ukraine and between Hamas and Israel, which have contributed to further economic instability in the global financial markets~~ . As a result, adequate additional financing may not be available to us when needed or on attractive terms. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or altogether terminate our research and development programs or future commercialization efforts. Raising additional capital may cause dilution to our stockholders and restrict our operations or require us to relinquish rights to our product candidates. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, including through third- party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest in our company may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights. If we raise additional capital through future collaborations, strategic alliances or third- party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves. Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations. We have incurred substantial losses since inception and do not expect to become profitable in the near future, if ever. In general, under Section 382 of the United States Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an " ownership change " is subject to limitations on its ability to utilize its pre- change **net operating losses (“** NOLs **”)** to offset future taxable income **. An ownership change for these purposes is generally defined as a greater than 50 % change, by value, in the equity ownership of a corporation over a 3- year period** . We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent changes in our stock ownership (some of which shifts are outside our control). As a result, if, and to the extent that we earn net taxable income, our ability to use our pre- change NOLs to offset such taxable income may be subject to limitations. For NOLs arising in tax years beginning after December 31, 2017, the Code limits a taxpayer' s ability to utilize NOL carryforwards to 80 % of taxable income. In addition, NOLs arising in tax years ending after December 31, 2017 **,** ~~44can~~ -- **can** be carried forward indefinitely, but carryback is generally prohibited. NOLs generated in tax years beginning before January 1, 2018 ~~will~~ **, are** not ~~be~~ subject to the **80 %** taxable income limitation, and NOLs generated in tax years ending before January 1, 2018 ~~will~~ **,** continue to have a two- year carryback and 20- year carryforward period. Deferred tax assets for NOLs **are** ~~will need to be~~ measured at the applicable tax rate in effect when the NOL is expected to be utilized. The limitations in the carryforward ~~/~~ **and** carryback periods, as well as the limitation on use of ~~NOLs for~~ NOLs arising in tax years beginning after December 31, 2017 **,** may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In order to realize the future tax benefits of our NOL carryforwards, we must generate taxable income, of which there is no assurance. Accordingly, we have provided a full valuation allowance for deferred tax assets as of December 31, **2024 and** 2023 ~~and 2022~~ . Risks Related to the Development and Commercialization of Our Product ~~CandidatesOur~~ **CandidatesWe received a Warning Letter from the FDA for our NDA filed in December 2023 for our AT- 007- 1002 study. Failure to resolve the matters addressed in the Warning Letter could negatively impact our company' s ability to undertake clinical trials in the future or timely complete future NDA submissions. In November 2024, we received a Warning Letter from the FDA relating to our AT- 007- 1002 study. The letter identified issues related to electronic data capture and also referred to a dosing error in the dose- escalation phase of our study resulting in slightly lower levels than targeted in a limited number of patients. We responded to the Warning Letter in a timely manner and our response contained various remediation measures. We are closely working with our clinical team, consultants, and employees to develop and implement a plan that addresses FDA' s concerns. Such actions have and will continue to increase our expenses, and the extent of those costs is still unknown. If we are unable to sufficiently establish**

to the FDA that current or future clinical trials conducted by us would be in accordance with FDA regulations, we may be subject to enforcement action by the FDA including being subject to the FDA' s Application Integrity Policy. This policy would require third- party validation of the integrity of the raw data underlying any of our future filings to the FDA before those filings would be accepted for consideration. Such a requirement would be onerous and require significant additional time and expense, including unforeseen costs, for the clinical development and potential approval of any product candidates that we are currently developing and may wish to develop in the future. These requirements would make it difficult for us to attempt to restart the development of any of our former product candidates or commence the development of any new product candidates. Further, we could be subject to additional actions from the FDA that may negatively impact our ability to enter into clinical trials or submit an NDA in the future. We recently received a Complete Response Letter from the FDA for our NDA for govorestat (AT- 007) for the treatment of Classic Galactosemia, one of our lead product candidates, and we are currently evaluating our development program for Classic Galactosemia and SORD Deficiency, and do not currently know if govorestat will ever receive regulatory approval for any indication, which is necessary before it can be commercialized. If we do not receive regulatory approval for govorestat (AT- 007) for the treatment of Classic Galactosemia or SORD Deficiency or any other indication and we are not able to commercialize govorestat, we may not generate revenue for several years, if at all, and we may never generate sufficient revenue to achieve and sustain profitability. We need approval from the FDA prior to marketing our product candidates in the U. S. In December 2023, we submitted our first NDA to the FDA seeking approval for govorestat. In February 2024, the FDA accepted the filing of the NDA and the NDA was granted Priority Review status. In November 2024, the FDA issued a Complete Response Letter for the NDA. The Complete Response Letter indicates that the FDA completed its review of the application and determined that is unable to approve the NDA in its current form, citing deficiencies in the clinical application and failure to reach statistical significance on primary endpoints. Following receipt of the Complete Response Letter, we also withdrew the Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for govorestat for the treatment of Classic Galactosemia, as we believed more time was needed to acquire further data to support a European MAA. We are in the planning stages of determining our next steps with respect to our govorestat development program. Further clinical development of govorestat for any indications may require us to complete additional and more extensive clinical trials, which will be costly and time consuming. The amount and timing of the increased costs related to our clinical trials is difficult to predict due to the uncertainty inherent in the timing of clinical trial initiations, the rate of patient enrollment and the detailed design of future trials. If we continue our clinical development program for govorestat, we may not obtain necessary approvals from the FDA even if our trials demonstrate favorable results. The data we collect from any additional clinical trials may not demonstrate sufficient safety and efficacy to support regulatory approval of govorestat in which case we would experience potentially significant delays in, or be required to abandon, development of that product candidate. If we continue our clinical development program for govorestat, we will have fewer resources to devote to the research and development of our other product candidates and development stage programs. If we decide to terminate any further development of govorestat, we will be dependent upon the success of our other product candidates in our pipeline or other compounds we may in- license and the size of the potential markets for such other product candidates may not be as significant as the potential markets for govorestat, and we may not be able to monetize it. Our other indications and development stage programs are in various stages of development. In light of recent regulatory developments, we will be closely examining the ongoing SORD Deficiency clinical development program and will continue to work with the FDA on the data needed to support an appropriate regulatory pathway for the drug, including ongoing work to provide the FDA with support for the potential use of the accelerated approval pathway for govorestat for the treatment of SORD Deficiency. We plan to meet with the FDA to discuss whether an NDA can be submitted based on the current data package and / or potential additional supporting data. However, there is no guarantee that the FDA will agree with this strategy, and the agency may require additional costly preclinical or clinical trials to support an NDA. There is also the risk that these additional trials will not be successful. Our future success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates. If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate product revenue will be adversely affected. We have invested a significant portion of our time and financial resources in the development of AT- 007, AT- 001 and AT- 003. Our business is dependent on our ability to successfully complete development of, obtain regulatory approval for, and, if approved, successfully commercialize our product candidates in a timely manner. We may face unforeseen challenges in our drug development strategy **, such as the Complete Response Letter received from the FDA for the NDA we submitted for govorestat** , and we can provide no assurances that our drug design will prove to be effective, that we will be able to take advantage of expedited regulatory pathways for any of our product candidates, or that we will ultimately be successful in our future clinical trials. We have not obtained regulatory approval for any product candidate, **our NDA seeking approval of AT- 007 for Classic Galactosemia received a Complete Response Letter and was not approved,** and it is possible that any product candidates we may seek to develop in the future will not obtain regulatory approval. Neither we nor any future collaborator is permitted to market any product candidates in the United States or abroad until we receive regulatory approval from the FDA or applicable foreign regulatory agency. The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign regulatory authorities is unpredictable and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions. Prior to obtaining approval to commercialize any product candidate in the United States or abroad, we must demonstrate ~~with~~

~~substantial evidence from well- controlled clinical trials, and~~ to the satisfaction of the FDA or comparable foreign regulatory authorities ~~,~~ that such product candidate is safe and effective for its intended uses. **The FDA requires " substantial evidence " to make a finding of effectiveness for any approval, including accelerated approval. Substantial evidence generally requires two adequate and well- controlled studies; however, in certain circumstances, substantial evidence may be based on a single, large, multicenter, adequate and well- controlled study together with confirmatory evidence to be sufficient.** Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe that the preclinical or clinical data for our product candidates are promising **and meet the applicable** ~~, such data may not be sufficient to support~~ approval ~~by~~ **standards,** the FDA and other regulatory authorities **may disagree, or it may no longer be acceptable to the FDA upon submission due to changes in regulatory standards** . The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post- approval, or it may object to elements of our clinical development program, requiring their alteration. Of the large number of products in development across the pharmaceutical industry, only a small percentage successfully complete the FDA or comparable foreign regulatory authorities approval processes and ~~are commercialized~~ **receiving marketing authorization** . The lengthy approval or marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval or marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. Even if we eventually complete clinical testing and receive approval of a new drug application ~~, or NDA,~~ or foreign marketing for our product candidates, the FDA or the comparable foreign regulatory authorities may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including ~~45post~~ -- **post** - market clinical trials. The FDA or the comparable foreign regulatory authorities also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or comparable foreign regulatory authorities may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would adversely impact our business and prospects. In addition, the FDA or comparable foreign regulatory authorities may change their policies, adopt additional regulations ~~or~~ **,** revise existing regulations **or guidance** or take other actions, which may prevent or delay approval of our future product candidates under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. **The development of our product candidates also may be delayed by other events beyond our control. For example, actions to limit federal agency budgets or personnel may result in reductions to the FDA' s budget, employees, and operations, as well as changes to FDA regulatory programs, all of which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates, undergo regulatory inspections or obtain regulatory approval for our product candidates.** Furthermore, even if we obtain regulatory approval for our product candidates, we will still need to develop a commercial organization, establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third- party and government payors, including government health administration authorities. If we are unable to successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business. **Changes in funding for the FDA and other government agencies and the implementation of tariffs could prevent new products and services from being developed or commercialized in a timely manner or at all, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, payment of user fees and reauthorization of user fee programs, staffing and other resource limitations, ability to hire and retain key personnel, as well as statutory, regulatory and policy changes. In addition, funding of other government agencies that support research and development activities that pertain to FDA review, such as research to understand new technologies or establish new standards, is subject to the political process, which is inherently fluid and unpredictable. Such government agencies also have been subject to reductions in funding and downsizing of agency staffing levels, which could materially impact our business and operations. The current administration has implemented or proposed policies that may affect the FDA review process, including efforts to downsize the federal workforce, remove job elimination protections for federal workers, limit certain communications, and potentially impact user fee reauthorization. If political pressure or global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. In addition, a portion of our supply chain is located in countries that may be subject to new or increased tariffs, which could lead to increased costs to us. This exposure to international trade policies poses a risk to our operations and our financial condition.** We or Advanz Pharma may fail to perform under any of the agreements entered into in connection with the partnership for **the potential** commercialization of AT- 007, which may subject us to liabilities, and we may fail to achieve anticipated benefits of the partnership. In January 2023, we announced a partnership with Advanz Pharma (~~" "~~ Advanz ~~" "~~) for **the potential** commercialization of AT- 007 (govorestat) in Europe, and entered into an Exclusive License and Supply Agreement (~~" the "~~ Advanz Agreement ~~" "~~) with Advanz. Under the terms of the Advanz Agreement, Advanz receives exclusive commercial rights in the European Economic Area, Switzerland, and the UK (~~the "~~ Territory ~~"~~) for AT- 007 in Galactosemia and SORD Deficiency, with certain rights to future indications for AT- 007 in the Territory. In return, we have the right to receive certain near- term development milestone payments upon clinical trial completion and marketing authorization in Europe as well as commercial sales milestones, which in the aggregate are expected to amount to over € 130 million. We also have the right to receive royalties on any future net sales of AT- 007 in the Territory of 20 %. The royalty rate will be payable

on a country- by- country basis until the later of (i) the expiration of the licensed patents covering the composition of matter of AT- 007, or (ii) 10 years after the European Medicines Agency' s grant of marketing authorization for AT- 007. The royalties are subject to certain deductions, including certain secondary finishing costs, certain step- in establishment costs and a portion of fees for any potential third- party patent licenses if applicable in the future. Following the initial term of the license, as described above, the royalty rate shall be reduced to 10 % and shall continue in perpetuity unless the Advanz Agreement is terminated in various circumstances in accordance with its terms. We will continue to be responsible for the development, manufacturing and supply of AT- 007, and Advanz will be responsible for packaging, distribution and commercialization in the Territory. The Advanz Agreement includes a sublicense under the 2016 Columbia Agreement and the 2020 Miami License Agreement. Our partnership with Advanz is subject to various risks, including **,** but not limited to **,** the following: • If Advanz breaches the contractual obligations owed to us pursuant to the Advanz Agreement or any related agreements, we could be exposed to commercial, regulatory or other liabilities. • We may be subject to liabilities in connection with the development, manufacturing and supply of AT- 007 under the Advanz Agreement, including with respect to the 2016 Columbia Agreement and the 2020 Miami License Agreement. • We may not be able to adequately protect our intellectual property or may become involved in intellectual property enforcement actions, which may cause us to incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and such litigation may divert the attention of our management and scientific personnel and adversely affect our development and commercialization efforts. ~~• 46 •~~ We may have limited control over the commercialization efforts of Advanz, and Advanz may fail to successfully sell and market AT- 007. • Our ability to receive certain economic benefits from the partnership, including the milestone payments and royalties, depends on certain contingencies beyond our control. • In certain circumstances, Advanz may exercise certain step- in rights, including the ability for Advanz to perform its own supply arrangements, and in some cases, specified development rights in the Territory and assignment of certain contract rights. In all such circumstances, Advanz must continue to pay royalties and milestone payments, but may recoup certain of its manufacturing and development establishment costs, and deduct such costs from royalties owed. Any of these factors could cause us to incur higher costs, disrupt the supply of our product candidates or approved products, delay **or prevent** the approval of our product candidates or prevent or disrupt the commercialization of our approved products. As a result, we may not achieve some or all economic benefits expected from the partnership. The development of additional product candidates is risky and uncertain, and we can provide no assurances that we will be able to replicate our approach to drug development for other disease indications. Efforts to identify, acquire or in- license, and then develop, product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our efforts may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development, approved products or commercial revenues for many reasons, including the following: • the methodology used may not be successful in identifying potential product candidates; • competitors may develop alternatives that render any product candidates we develop obsolete; • any product candidates we develop may be covered by third parties' patents or other exclusive rights; • a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria; • a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third- party payors. We have limited financial and management resources and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. In addition, we may not be successful in replicating our approach to drug development for other disease indications. If we are unsuccessful in identifying and developing additional product candidates or are unable to do so, our business may be harmed. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals. Success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies and Phase 1 clinical trials are primarily designed **and operate** to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through earlier clinical trials. ~~47In~~ **In** addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be ~~unable to~~ **unsuccessful in** ~~design~~ **designing** and ~~execute~~ **executing** a clinical trial to support regulatory approval ~~.~~ Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving promising results in preclinical testing and earlier clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects. Clinical drug development involves a lengthy and expensive process. We may incur additional costs and encounter substantial delays or difficulties in our clinical trials. We may not commercialize, market, promote or sell any product candidate

without obtaining marketing approval from the FDA or other comparable regulatory authority, and we may never receive such approvals **, particularly following the recent Complete Response Letter received from the FDA for the NDA for govorestat for the treatment of Classic Galactosemia** . It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. We may experience numerous unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including the following: • delays in reaching a consensus with regulatory authorities on the design or implementation of our clinical trials; • regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites; • **FDA requirements for the approval of govorestat for any indication; •** the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post- treatment follow- up or we may fail to recruit suitable patients to participate in a trial; • clinical trials of our product candidates may produce negative or inconclusive results; • imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities; • occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; • **deviations from GCP or clinical trial protocols, data integrity issues and other issues that could affect the data or other results of a clinical trial, the safety or efficacy of a product candidate or a product candidate' s review or approval by regulatory authorities; •** changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or • we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs. Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales or other sources. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified ~~48product~~ -- **product** candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring competing drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects. Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may: • **receive a new warning letter from the FDA, which can damage our reputation and prevent the continuance of our clinical trials; •** be delayed in obtaining marketing approval, or not obtain marketing approval 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, including in the form of a risk evaluation and mitigation strategy, or REMS; • be subject to additional post- marketing testing requirements; • be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; • have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a **new or** modified REMS; • be subject to the addition of labeling statements, such as warnings or contraindications; • be sued; or • experience damage to our reputation. Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all. Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA' s ~~current Good Clinical Practice, or~~ GCP ~~,~~ regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our investigational new drug applications, or INDs, or the conduct of these trials. ~~Therefore~~ **In November 2024** , ~~we~~ **the FDA issued a Complete Response Letter for our NDA seeking approval of govorestat for the treatment of Classic Galactosemia citing deficiencies in the clinical application. We** cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed. All of our current product candidates that have proceeded to clinical trials target inhibition of aldose reductase. There can be no assurance that aldose reductase inhibitors will ever receive regulatory approval. All of our current product candidates that have proceeded to clinical trials target inhibition of the aldose reductase enzyme. **The FDA may not agree with this proposed mechanism of action for the indications we are pursuing, which could impact the amount of evidence the FDA requires to support marketing approval.** There are no currently approved aldose reductase inhibitors on the market outside of Japan, India **,** and China, and there can be no assurance that aldose reductase inhibitors will ever receive regulatory approval in ~~all~~ other countries, including the United States. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off- target safety effects. Our current product candidates ~~, including AT- 007, AT- 001 and AT- 003,~~ may face similar or different challenges that prevent their successful commercialization. We may not be able to obtain or maintain rare pediatric disease designation or exclusivity for our product candidates, which could

limit the potential profitability of our product candidates. We have obtained orphan drug designation and rare pediatric disease designation, from the FDA for AT- 007 for the treatment of Galactosemia and PMM2- CDG. The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is defined as a disease or condition that either affects fewer than 200, 000 individuals in the United States, or if it affects more than 200, 000 individuals, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United ~~49States~~ -- **States** . Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. For the purposes of the rare pediatric disease program, a " rare pediatric disease " is a serious or life- threatening disease in which the serious or life- threatening manifestations primarily affect individuals aged from birth to 18 years or a rare disease or conditions within the meaning of the Orphan Drug Act. Under the FDA' s rare pediatric disease priority review voucher, or RPD- PRV, program, upon the approval of an NDA for the treatment of a rare pediatric disease, the sponsor of such application ~~would~~ **may** be eligible for an RPD- PRV that can be used to obtain priority review for a subsequent NDA **or Biologics License Application (BLA)** . ~~The~~ **A rare pediatric disease designation does not guarantee that a** sponsor **will receive a PRV upon approval** of ~~the~~ **its** application **. If an** ~~may transfer (including by sale) the~~ RPD- PRV ~~to another sponsor~~ **is received, it may be sold or transferred an unlimited number of times** . ~~The~~ **However, the FDA' s rare pediatric disease priority** voucher **program began to sunset on December 20** ~~may be further transferred any number of times before the voucher is used~~ , **2024, upon** ~~as long as the sponsor making the transfer has not yet submitted the application.~~ Congress ~~has extended~~ **' failure to pass a continuing resolution package that included its reauthorization. Under** the **amended statutory sunset provisions, after December 20, 2024, the FDA may award an** RPD- PRV ~~program until~~ **for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After** September 30, ~~2024, with potential for vouchers to be granted until~~ 2026 **, the FDA may not award any rare pediatric disease PRVs** . **Congress may vote to reauthorize** ~~This~~ **this** program ~~has been subject to criticism~~ , **but** ~~including by the FDA. As such it~~ **its future remains unknown** ~~is possible that even though we have obtained qualification for a RPD- PRV, the program may no longer be in effect~~ at ~~the~~ **this** time ~~of approval. Also, although priority review vouchers may be sold or transferred to third parties, there is no guaranty that we will be able to realize any value if we obtained, and subsequently were able to sell a priority review voucher. The RPD- PRV program is currently scheduled to sunset as of September 30, 2026~~ . A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval. We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened. We **also are unable to predict the potential changes in regulatory interpretations or agency funding or staffing that may impact the FDA' s use or implementation of the Breakthrough Therapy designation. We** have sought, and may in the future seek, fast track designation from the FDA for our product candidates. Even if granted, fast track designation may not actually lead to a faster development, regulatory review or approval process. If a product candidate is intended for the treatment of a serious or life- threatening condition and demonstrates the potential to address unmet needs for this condition, the sponsor may apply for FDA fast track designation. If fast track designation is obtained, the FDA may prioritize interactions with the sponsor concerning the designated development program and initiate review of sections of an NDA before the application is complete, known as " rolling review. " Fast track designation would not ensure that we would experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we would ultimately obtain regulatory approval. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. ~~50We intend~~ **We also are unable** to **predict the potential changes in regulatory interpretations or agency funding or staffing that may impact the FDA' s use or implementation of the fast track designation. We may** seek approval from the FDA ~~through~~ **under** the ~~use of~~ accelerated ~~registration~~ **approval** ~~pathways~~ **pathway** . If we are unable to obtain **accelerated** approval ~~under an accelerated pathway~~ , we may be required to conduct additional preclinical studies or clinical trials, which could increase the expense of obtaining, reduce the likelihood of obtaining and / or delay the timing of obtaining, necessary marketing approvals. Even if we receive **accelerated** approval from the FDA **for a product candidate** ~~to utilize an accelerated registration pathway~~ , if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA may seek to withdraw accelerated approval. We intend to seek ~~an~~ **efficient pathways to approval for our product candidates, which may include the** accelerated approval ~~development~~ pathway ~~for our product candidates~~ . Under the accelerated approval provisions of the Federal Food, Drug, and Cosmetic Act, or the FDCA, and the FDA' s implementing

regulations, the FDA may grant accelerated approval to a product designed to treat a serious or life- threatening condition that provides meaningful therapeutic advantage over available therapies and demonstrates an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval development pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. **Products approved under the accelerated approval pathway are still required to meet the evidentiary standards for approval, including substantial evidence of effectiveness based on adequate and well- controlled studies.** If granted, accelerated approval is contingent on the sponsor' s agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug' s clinical profile or risks and benefits for accelerated approval. The FDA ~~may require~~ **has indicated its general expectation** that any such confirmatory studies be initiated or substantially underway prior to the submission of an application for accelerated approval **, and issued guidance as to what constitutes such a study being " underway** . **"** If such post- approval studies fail to confirm the drug' s clinical profile or risks and benefits, the FDA may withdraw its approval of the drug. The Food and Drug Omnibus Reform Act, or FDORA, which was signed into law on December 29, 2022, made amendments to the accelerated approval program, among them new requirements relating to post- approval studies and enhanced enforcement and withdrawal authorities for the FDA, including in the event that a sponsor fails to comply with applicable requirements under the program. **We** ~~Because we are still in early stages of our clinical trials, we~~ can provide no assurances that our biomarker- based approach will be successful in demonstrating a **predictive benefit in** ~~causal link to the~~ relevant **clinical** outcomes we are evaluating. If our approach is not successful, we may be required to conduct longer **, different, or additional** clinical trials **, which also may fail to confirm clinical benefit** . If we choose to pursue accelerated approval, we intend to seek feedback from the FDA or will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that, after our evaluation of the feedback from the FDA or other factors, we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. **Submitting** ~~Furthermore, even if we submit~~ an application for accelerated approval, **does** ~~there can be no~~ **not** ~~assurance~~ --- **assure** that the application will be accepted or that approval will be granted on a timely basis, or at all. The FDA also could require us to conduct further studies or trials prior to considering our application or granting approval of any type. We might not be able to fulfill the FDA' s requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate ~~would~~ **may** result in a longer time period to commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace. Even if we receive accelerated approval from the FDA, we will be subject to rigorous post- marketing requirements, including the completion of confirmatory post- market clinical trial (s) to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw accelerated approval for multiple reasons, including if we fail to conduct any required post- market study with due diligence, a post- market study does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false or misleading. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate that we may choose to develop would result in a longer time period prior to commercializing such ~~51product~~ -- **product** candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace. Enrollment and retention of patients in clinical trials is an expensive and time- consuming process and could be delayed, made more difficult or rendered impossible by multiple factors outside our control. Identifying and qualifying patients to participate in our clinical trials is critical to our success. We may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval of our product candidates. Even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data, the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the trial. Because our focus includes rare disorders, there are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost- effective manner. Accordingly, enrollment of our clinical trials could take significantly longer than projected, which would delay any potential approval of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials. Our efforts to build relationships with patient communities may not succeed, **particularly following the Complete Response Letter for govorestat for Classic Galactosemia and Warning Letter relating to our AT-007- 1002 study received from the FDA in November 2024,** which could result in delays in patient enrollment in our clinical trials. Any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates or could render further development impossible. In addition, we may rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to ensure their actual performance. ~~For additional information regarding delays in~~

~~enrollment and retention of patients, see " Risks Related to Our Business Operations, Employee Matters and Managing Growth — Our business may be adversely affected by the coronavirus outbreak. "~~ Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval. During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects or patients. Many times, side effects are only detectable after investigational drugs are tested in large- scale pivotal trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates have side effects or cause serious or life- threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition. ~~52Interim --~~ **Interim** , " top- line " and preliminary data from our clinical trials that we **have** ~~announce~~ **announced** or ~~publish~~ **published** ~~from time to time~~ **, has changed and** may **continue to** change as more patient data ~~become~~ **becomes** available and are subject to audit and verification procedures that **has resulted and** could **in the future** result in material changes in the final data. **We have** ~~From time to time, we may publish~~ **published** interim, " top- line " or preliminary data from our clinical trials **and may continue to do it from time to time** . Interim data from clinical trials that we **have completed and** may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues ~~and~~ **,** more patient data become available **, and / or additional analyses are conducted, as has occurred in the past** . Preliminary or " top- line " data ~~also~~ remain subject to **new or further** audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data **and results** are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly **. For example, in February 2024, we announced results from a group- level, interim analysis of 12- month data in the Phase 2 / 3 INSPIRE trial studying AT- 007 for SORD Deficiency. Our review and analyses of these data are ongoing** . The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we believe they are or any approval we obtain is based on a narrower definition of the patient population, our business may suffer. We currently focus our drug development on product candidates for the treatment of diseases with high unmet medical need. Our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our product candidates. Our estimates of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and analyses. These estimates have been derived from a variety of sources, including the scientific literature, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of the diseases we are targeting. The number of patients may turn out to be lower than expected. Likewise, the potentially addressable patient population for each of our product candidates may be limited or may not be receptive to treatment with our product candidates, and new patients may become increasingly difficult to identify or access. If the market opportunities for our product candidates are smaller than we estimate, we may not be able to achieve our forecast revenue, which could hinder our business plan and adversely affect our business and results of operations. We ~~may~~ face ~~substantial~~ competition, which may result in others developing or commercializing drugs before or more successfully than us. The development and commercialization of new drugs is highly competitive. We ~~may~~ face ~~potential~~ competition with respect to our current product candidates and may face competition with respect to any other product candidates that we may seek to develop or commercialize in the future from pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research institutions. Our competitors may have an advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts and relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed. As a result of these factors, our competitors may obtain regulatory approval of their drugs before we are able to, which may limit our ability to develop or commercialize our product candidates. Our competitors may also develop therapies that are safer, more effective, more widely accepted or less expensive than ours, and may also be more successful than we are in manufacturing and marketing their drugs. These advantages could render our product candidates obsolete or non- competitive before we can recover the costs of such product candidates' development and commercialization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These ~~53third --~~ **third** - parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. We may explore strategic collaborations that may never materialize or we may be required to relinquish important rights to and control over the development and commercialization of our product candidates to any future collaborators. Over time, our business strategy

includes acquiring or in- licensing additional product candidates for treatments of diseases with high unmet medical need. As a result, we ~~intend to~~ **expect that we may** periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. These strategic collaborations may include partnerships with large strategic partners, particularly for the development of DPN treatments using AT- 001. At the current time however, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic collaborations because of the numerous risks and uncertainties associated with establishing them. Future collaborations could subject us to a number of risks, including: • we may be required to undertake the expenditure of substantial operational, financial and management resources; • we may be required to issue equity securities that would dilute our stockholders' percentage ownership of our company; • we may be required to assume substantial actual or contingent liabilities; • we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our product candidates; • strategic collaborators may select indications or design clinical trials in a way that may be less successful than if we were doing so; • strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing; • strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs; • strategic collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products; • disputes may arise between us and our strategic collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management' s attention and consumes resources; • strategic collaborators may experience financial difficulties; • **changes in the collaborator' s strategic focus or available funding; •** strategic collaborators may not properly maintain, enforce 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 strategic collaborator' s business strategy may adversely affect a strategic collaborator' s willingness or ability to complete its obligations under any arrangement; • strategic collaborators could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; ~~and~~ • **collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies; •** strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates **; • collaborators may not perform their obligations as expected; and • other factors, such as an acquisition or business combination, that divert resources or create competing priorities** . ~~54Even~~ -- **Even** if any product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third- party payors or others in the medical community necessary for commercial success. Even if any product candidates receive marketing approval, they may fail to gain market acceptance by physicians, patients, third- party payors and others in the medical community. If such product candidates do not achieve an adequate level of acceptance, we may not generate significant drug revenue and may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to: • the convenience and ease of administration compared to alternative treatments and therapies; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the efficacy and potential advantages compared to alternative treatments and therapies; • the effectiveness of sales and marketing efforts; • the strength of our relationships with patient communities; • the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments; • our ability to offer such drug for sale at competitive prices; • the strength of marketing and distribution support; • the availability of third- party coverage and adequate reimbursement; • the prevalence and severity of any side effects; and • any restrictions on the use of the drug together with other medications. Our efforts to educate physicians, patients, third- party payors and others in the medical community on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our product candidates. Because we expect sales of our product candidates, if approved, to generate substantially all of our revenues for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business. Even if we obtain regulatory approvals for our product candidates, they will remain subject to ongoing regulatory oversight. Even if we obtain regulatory approvals for our product candidates, such approvals will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record keeping and submission of safety and other post- market information. Any regulatory approvals that we receive for our product candidates may also be subject to a **risk evaluation and mitigation strategy (** REMS **)** , limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. Such regulatory requirements may differ from country to country depending on where we have received regulatory approval. In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring

withdrawal of the drug from the market or suspension of manufacturing. If we **or our contract manufacturers or partners** fail to comply with applicable regulatory requirements following approval of our product candidates, a regulatory authority may, among other actions: • issue an untitled letter or warning letter asserting that we are in violation of the law; • ~~55 •~~ seek an injunction or impose administrative, civil or criminal penalties or monetary fines; • suspend or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve a pending NDA or comparable foreign marketing application or any supplements thereto submitted by us or our partners; • restrict the marketing or manufacturing of the drug; • seize or detain the drug or otherwise require the withdrawal of the drug from the market; • refuse to permit the import or export of product candidates; or • refuse to allow us to enter into supply contracts, including government contracts. Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product' s approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted off- label uses may be subject to significant civil, criminal and administrative penalties. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and harm our business **. Further, if we are not able to maintain regulatory compliance with the FDCA, Cures Act, or other applicable requirements, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects** , financial condition ~~,~~ **and** results of operations ~~and prospects~~ . The FDA' s and other regulatory authorities' policies may change and additional ~~laws or~~ government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. ~~If~~ **For example, on June 28, 2024, the U. S. Supreme Court, in Loper Bright Enterprises v. Raimondo, overturned long- standing precedent regarding the deference courts** ~~we~~ **owe** ~~are not able~~ to ~~maintain~~ **agencies' interpretation of ambiguous statutes in their rulemaking. While the impact of the Loper Bright decision on our business and** regulatory ~~compliance~~ **strategy is unknown, the decision generally may, among other things, increase the frequency of challenges to decisions and rulemaking of health regulators, including FDA determinations of drug approval and market exclusivity and the Centers for Medicare & Medicaid Services' rules regarding reimbursement, and also impact the speed at which such health regulators make decisions and issue regulations. Furthermore, beginning in February 2025, the Trump administration has downsized and terminated significant numbers of employees at the FDA and the NIH, along** with ~~the FDCA, Cures Act, or~~ other ~~applicable requirements, we may lose~~ **federal agencies. We cannot predict the effect that** any **such restructuring** ~~marketing approval that we~~ may have **on** ~~obtained and we may not achieve or sustain profitability, which would adversely affect~~ our business ~~, prospects, financial condition and results of operations~~ . In addition, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the U. S. administration may impact our business and industry. It is difficult to predict how executive actions, including executive orders, may be implemented and the extent to which they will affect the FDA' s ability to exercise its regulatory authority. If legislative, administrative or executive actions impose constraints on the FDA' s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing them, if and when they are approved. To successfully commercialize any product candidate that may result from our development programs, we will need to build out our sales and marketing capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any product candidate we may develop will be expensive and time- consuming and could delay any drug launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may seek to enter into collaborations with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we may be unable to generate sufficient revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well- funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We will likely also face competition if we seek third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third- party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies. ~~56Even --~~ **Even** if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval outside the United States, which would limit our market opportunities. Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable foreign regulatory authorities also must approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any product candidates, if approved, is also subject to approval. Obtaining approval for our product candidates in the European Union from the European Commission following the opinion of the European Medicines Agency, or the EMA, is a lengthy and expensive process. Even if a product candidate is approved, the EMA may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require

expensive and time- consuming additional clinical trials or reporting as conditions of approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. **Following receipt of the Complete Response Letter for govorestat for the treatment of Classic Galactosemia, we also withdrew the MAA to the EMA for govorestat for the treatment of Classic Galactosemia, which may result in further delays, difficulties and costs to support a European MAA for govorestat.** Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our product candidates may be withdrawn. If we fail to comply with the applicable regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects could be harmed. If we commercialize our product candidates outside the United States, a variety of risks associated with international operations could harm our business. ~~We~~ **If we obtain regulatory and marketing approval in the United States for any product candidate, we** intend to seek approval to market our product candidates outside the United States ~~, and may do so for future product candidates~~. If we market approved products outside the United States, we expect that we will be subject to additional risks in commercialization, including: • different regulatory requirements for approval of therapies in foreign countries; • reduced protection for intellectual property rights; • unexpected changes in tariffs, trade barriers and regulatory requirements; • economic weakness, including inflation, or political instability in particular foreign economies and markets; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; • foreign reimbursement, pricing and insurance regimes; • workforce uncertainty in countries where labor unrest is more common than in the United States; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geopolitical actions, including war and terrorism, international hostilities, or natural disasters including earthquakes, typhoons, floods and fires. We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by many of the individual countries in which we may operate, with which we will need to comply. Many biopharmaceutical companies have found the process of marketing their products in foreign countries to be challenging.

 liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any product candidate that we may develop. If we cannot successfully defend ourselves against claims that any such product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidate that we may develop; • loss of revenue; • substantial monetary awards to trial participants or patients; • significant time and costs to defend the related litigation; • withdrawal of clinical trial participants; • increased insurance costs; • the inability to commercialize any product candidate that we may develop; and • injury to our reputation and significant negative media attention. Any such outcomes could negatively impact our business, financial condition, results of operations and prospects. Our insurance policies may be inadequate and potentially expose us to unrecoverable risks. Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage and insurers may not respond as we intend to cover insurable events that may occur. We have observed rapidly changing conditions in the insurance markets relating to nearly all areas of traditional corporate insurance. Such conditions have resulted in higher premium costs, higher policy deductibles, and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability. Risks Related to Regulatory ComplianceOur relationships with customers, physicians, and third- party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. Healthcare providers, physicians and third- party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third- party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti- Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations. Ensuring that our business arrangements with third- parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government- funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government- funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to

healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace **. We may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, and depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA** . Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell profitably, if approved. Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third- party payors, including government health administration authorities, managed care organizations and other private health insurers. Third- party payors decide which therapies they will pay for and establish reimbursement levels. While no uniform policy for coverage and reimbursement exists in the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor- by- payor basis. Therefore, one payor' s determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third- party payor' s decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a payor' s list of covered drugs, or formulary, generally determines the co- payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third- party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our product candidates, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates that we develop. **Due to general uncertainty with respect to the current legal, regulatory and policy environment, we are unable to predict the impact of any future legislative, regulatory, third- party payor or policy actions. If enacted, we and any third parties we might engage may be unable to adapt to any changes implemented as a result of such measures, and we could face difficulties in maintaining or increasing profitability or otherwise experience a material adverse impact on our business, financial condition and results of operations.** Healthcare reform measures may have a negative impact on our business and results of operations. In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes, as well as judicial challenges, regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post- approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. **The increased emphasis on managed healthcare in the U. S. and on country-specific and national pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing coverage and / or reimbursement controls and measures, could have a material adverse impact on our net product revenues and results of operations.** In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, **since** ~~the Medicare Prescription Drug, Improvement, and Modernization Act of~~ 2003, ~~or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded~~ Medicare coverage for drug purchases by the elderly ~~and introduced~~ **have been subject to** a ~~new~~ reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the ~~59number~~ -- **number** of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the **Managed Medical Assistant (** MMA **) program** applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. Further, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the PPACA, was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to executive, judicial and Congressional challenges. For example, ~~the Tax Cuts and Jobs Act of 2017, or Tax Act includes~~ a ~~provision that~~

~~repealed, effective January 1, 2019, the tax- based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the " individual mandate. ". On December 14, 2018, a U. S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the individual mandate was a critical and inseverable feature of the PPACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the PPACA were invalid as well. The U. S. Supreme Court heard arguments in the case in November 2020 and issued its decision in June 2021, ruling that the plaintiffs lacked the standing to challenge the individual mandate provision. In so holding, the Supreme Court did not consider larger constitutional questions about the validity of this provision or the validity of the PPACA in its entirety. Another~~ case challenging the PPACA' s requirement that insurers cover certain preventative services is currently pending before the ~~same~~ U. S. District Court **for** ~~Judge in~~ the Northern District of Texas ~~who ruled against the individual mandate in 2018~~ . In ~~September~~ **March** ~~2022~~ **2023** , the judge **struck down the requirement, and, on appeal, in June 2024 the U. S. Court of Appeals for the Fifth Circuit** held **, among other things,** that the PPACA **' s** requirement ~~to~~ **that group health plans and health insurance issuers** cover certain preventative services ~~violated~~ **without cost- sharing is unconstitutional. The parties have petitioned to appeal the case to** the U. S. **Supreme Court** ~~Constitution and set a schedule for additional briefing~~ , which ~~was completed~~ **granted certiorari** in January ~~2023~~ **2025** . **It** ~~In March 2023, the judge struck down the requirement with immediate nationwide effect by ruling, in part, that members of a panel charged under the PPACA with recommending preventative services coverage had been appointed in an unconstitutional manner. Parties on both sides of the lawsuit have appealed this ruling, and in June 2023 the U. S. Court of Appeals for the Fifth Circuit approved an agreement by the parties on a stay of the lower court' s ruling pending the appeal. Oral arguments have been scheduled for March 2024, and it~~ is unclear how this decision, subsequent decisions and appeals, or any potential future litigation **, executive orders or other actions by the current administration,** and other efforts to repeal and replace the PPACA will impact the PPACA. Congress may consider additional legislation to repeal or repeal and replace other elements of the PPACA. We continue to evaluate the effect that the PPACA and its possible repeal and replacement may have on our business and the potential profitability of our product candidates. Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2 % per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the **Bipartisan Budget Act (** BBA **)** , which will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. **The current Trump administration has taken additional action to limit or change healthcare policies pursued by the prior Biden Administration. For example, President Trump rescinded an executive order issued by former President Biden, pursuant to which the Center for Medicare and Medicaid Innovation (CMMI) created three drug pricing experiments, and it is unclear whether CMMI will continue to pursue some or any of these models or that other changes may occur under the current administration. Beginning in February 2025, the Trump administration has downsized and terminated significant numbers of employees at the FDA and the NIH, along with other federal agencies. We cannot predict the impact that any such restructuring may have on our business.** Additional changes that **may** affect our business include the expansion of programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015. At this time, the full impact of the introduction of the Medicare quality payment program on overall physician reimbursement is unclear. Further, in the United States there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. While some of the proposed measures will require authorization through additional legislation to become effective, the U. S. Congress have indicated that they will continue to seek new legislative and / or administrative measures to control drug costs. For example, the Inflation Reduction Act of 2022 also seeks to reduce prescription drug costs by, among other provisions, allowing Medicare to negotiate prices for certain high- cost ~~60prescription~~ -- **prescription** drugs in Medicare Parts B and D, imposing an excise tax on pharmaceutical manufacturers that refuse to negotiate pricing with Medicare, requiring inflation rebates to limit annual drug price increases in Medicare, redesigning the Medicare Part D formula, and limiting cost- sharing for insulin products. It is unclear **how the IRA will be effectuated or changed under the new Trump Administration or the degree of impact that the IRA may ultimately have upon our business, or** whether additional drug pricing and other healthcare reform measures will be enacted, and if enacted, what effect they would have on our business. We expect that additional U. S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U. S. federal government will pay for healthcare products and services, which could result in reduced demand for our current or any future product candidates or additional pricing pressures. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing or new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future product candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. ~~Further~~ **At the state level** , **legislatures and regulatory agencies have increasingly passed legislation and implemented regulations designed to control drug pricing, including restrictions** on **pricing** ~~May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017,~~ or **reimbursement at** the **state government level** ~~Right to Try Act~~ , **limitations on discounts to patients** ~~was signed into law. The law~~ , ~~among~~ **advance notices of price increases, marketing cost disclosure and transparency measures, and, in some cases, policies to encourage importation from** other ~~things,~~

~~provides a~~ **countries (subject to** federal ~~framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA~~ approval **)** ~~. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials~~ and **bulk purchasing** ~~without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act~~ . We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on demand for our product candidates if they are approved. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. Risks Related to Our Dependence on Third ~~PartiesWe~~ **PartiesOne** ~~intend~~ **of our clinical investigators received a warning letter from the FDA following a site inspection. Failure** to **resolve the matters addressed in the warning letter and any similar issues at other clinical trial sites could negatively impact the continuance of our govorestat clinical program, our ability to rely on the data collected in our clinical trials for regulatory submissions and approval, and our ability to undertake clinical trials in the future or timely complete future NDA submissions. In November 2024, one of our clinical investigators received a warning letter (Clinical Investigator Warning Letter) from the FDA relating to our AT- 007- 1002 study, following a site inspection in April 2024. The inspection was conducted as a part of the FDA' s Bioresearch Monitoring Program. The Clinical Investigator Warning Letter identified issues with the clinical investigator' s compliance with the FDA requirements and regulations governing clinical investigations. Specifically, the Clinical Investigator Warning Letter cited deviations from the investigational plan. If we are unable to sufficiently establish to the FDA that our current or future clinical trials are and will be conducted in accordance with FDA requirements, Applied (and our clinical investigators) may be subject to additional FDA enforcement action including being subject to the FDA' s Application Integrity Policy. For more information on the Warning Letter we received from the FDA and the implications of being subject to the FDA' s Application Integrity Policy, please see " Risks Related to Our Operations, Employee Matters and Managing Growth – We received a Warning Letter from the FDA for our NDA filed in December 2023 for our AT- 007- 1002 study. Failure to resolve the matters addressed in the Warning Letter could negatively impact our company' s ability to undertake clinical trials in the future or timely complete future NDA submissions. " We** rely on third parties to produce clinical and commercial supplies of our product candidates. We do not own or operate facilities for drug manufacturing, storage and distribution, or testing. We are dependent on third parties to manufacture the clinical supplies of our current and any future product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP requirements, for manufacture of both active drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure and / or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third- party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. We also intend to rely on third- party manufacturers to supply us with sufficient quantities of our product candidates to be used, if approved, for commercialization. We do not yet have a commercial supply agreement for commercial quantities of drug substance or drug product. If we are not able to meet market demand for any approved product, it would negatively impact our ability to generate revenue, harm our reputation, and could have an adverse effect on our business and financial condition. ~~61Further~~ -- **Further** , our reliance on third- party manufacturers entails risks to which we ~~would~~ **may** not be subject if we manufactured product candidates ourselves, including: • inability to meet our product specifications and quality requirements consistently; • delay or inability to procure or expand sufficient manufacturing capacity; • issues related to scale- up of manufacturing; • costs and validation of new equipment and facilities required for scale- up; • our third- party manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately; • our third- party manufacturers may fail to comply with cGMP requirements and other inspections by the FDA or other comparable regulatory authorities; • our inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all; • breach, termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; • reliance on single sources for drug components; • lack of qualified backup suppliers for those components that are currently purchased from a sole or single- source supplier; • **diminished numbers of FDA inspectors available to conduct pre- approval inspections may slow the pre- approval inspection process and delay review and / or approval of our applications; •** our third- party manufacturers may not devote sufficient resources to our product candidates; • we may not own, or may have to share, the intellectual property rights to any improvements made by our third- party manufacturers in the manufacturing process for our product candidates; • operations of our third- party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and • carrier disruptions or increased costs that are beyond our control. In addition, if we enter into a strategic collaboration with a third- party for the commercialization of our current or any future product candidates, we will not be able to control the amount of time or resources

that they devote to such efforts. If any strategic collaborator does not commit adequate resources to the marketing and distribution of our product candidates, it could limit our potential revenues. Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize our current or any future product candidates once approved. Some of these events could be the basis for FDA action, including injunction, request for recall, seizure, or total or partial suspension of production. Our business involves the use of hazardous materials and we and our third- party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do, or interrupt our, business. Our research and development activities and our third- party manufacturers' and suppliers' activities involve the generation, storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds and wastes. We and our manufacturers and suppliers are subject to environmental, health and safety laws and regulations governing, among other matters, the use, manufacture, generation, storage, handling, transportation, discharge and disposal of these hazardous materials and wastes and worker health and safety. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination or injury, which could result in an interruption of our commercialization efforts, research and development efforts and business operations, damages and significant cleanup costs and liabilities under applicable environmental, health and safety laws and regulations. We also cannot guarantee that the safety procedures utilized by our third- party manufacturers for handling and disposing of these materials and wastes generally comply with the standards prescribed by these laws and regulations. We may be held liable for any resulting damages, costs or liabilities, which could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and / or interrupt our business operations. Furthermore, environmental, health and safety laws and regulations are complex, change frequently and have tended to become more ~~62stringent~~ -- **stringent** . We cannot predict the impact of such changes and cannot be certain of our future compliance. Failure to comply with these environmental, health and safety laws and regulations may result in substantial fines, penalties or other sanctions. We do not currently carry environmental insurance coverage. We rely on third- parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business. We do not currently have the ability to independently conduct any clinical trials. We **have relied and** intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we **are** ~~will be~~ responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with the good laboratory practices, or GLPs, and GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we rely on CROs to conduct GCP- compliant clinical trials, we remain responsible for ensuring that each of our ~~GLP~~ preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations. If we or our CROs fail to comply with GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process. **In particular, one of our clinical investigators for the ACTION- Galactosemia Kids (AT- 007- 1002) received the Clinical Investigator Warning Letter following an inspection conducted by the FDA at her clinical site in April 2024. The Clinical Investigator Warning Letter identified issues with the clinical investigator' s compliance with the FDA requirements and regulations governing clinical investigations. Specifically, the Clinical Investigator Warning Letter cited deviations from the investigational plan. For more information, please see " Risks Related to Our Dependence on Third Parties". Failure to resolve the matters addressed in the warning letter and any similar issues at other clinical trial sites could negatively impact the continuance of our govorestat clinical program, our ability to rely on the data collected in our clinical trials for regulatory submissions and approval, and our ability to undertake clinical trials in the future or timely complete future NDA submissions. " Further, we experienced issues related to data collection, management, and retention with one of our vendors for AT- 007- 1002 that were raised in the Warning Letter to Applied. This vendor had a role in the Phase 2 / 3 INSPIRE trial (AT- 007- 1005) for SORD Deficiency; we are still investigating whether any issues with this vendor have impacted the INSPIRE trial. In addition, a clinical trial site for the SORD Deficiency trial outside of the United States is in the process of responding to an inspection by local authorities, and we are evaluating the potential impact of such inspection on the data.** Our reliance on third parties to conduct clinical trials ~~will result~~ **results** in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with CROs and other third parties can be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Such parties may: ● have staffing difficulties; ● fail to comply with contractual obligations; ● experience legal or regulatory compliance issues; or ● undergo changes in priorities or become financially distressed. These factors may adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or fail to comply with regulatory requirements, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory

approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed. While we **have and** will have agreements governing their activities, our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our relationship with any of these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial ~~63cost~~ -- **cost** and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. While we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our product candidates. Risks Related to Our Intellectual PropertyLicensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If we breach our license agreements with Columbia University or any of the other agreements under which we acquired, or will acquire, the intellectual property rights to our product candidates, we could lose the ability to continue the development and commercialization of the related product. The licensing of intellectual property is of critical importance to our business and to our current and future product candidates, and we expect to enter into additional such agreements in the future. In particular, our current product candidates AT- 007, AT- 001 and AT- 003 are dependent on our license agreement with The Trustees of Columbia University in the City of New York, or Columbia University. Pursuant to that license agreement with Columbia University, or the 2016 Columbia Agreement, Columbia University granted us an exclusive license under two important patent families, and a nonexclusive license to certain know- how, owned by Columbia University to develop, manufacture or commercialize certain compounds, including AT- 001, AT- 003 and AT- 007, for the diagnosis and treatment of human and animal diseases and conditions. The license grant is worldwide, with the exception of the patent family that covers AT- 001 and AT- 003. The license grant for the patent family that covers AT- 001 and AT- 003 excludes patent rights in China, Taiwan, Hong Kong and Macao, which Columbia University has exclusively licensed to a third- party. We cannot prevent Columbia University' s third- party licensee from developing, manufacturing or commercializing certain compounds, including AT- 001 and AT- 003, but not including AT- 007, in China, Taiwan, Hong Kong and Macao, and we cannot develop, manufacture or commercialize AT- 001 or AT- 003 in these territories, which could have a negative effect on our business. We do not have the right to control the preparation, filing, prosecution and maintenance of patents and patent applications covering the technology that we license under either of the Columbia Agreements. Therefore, we cannot always be certain that these patents and patent applications will be prepared, filed, prosecuted and maintained in a manner consistent with the best interests of our business. Although we have a right to have our comments considered in connection with the prosecution process, if Columbia University fails to prosecute and maintain such patents, or loses rights to those patents or patent applications as a result of its control of the prosecution activities, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. If we fail to meet our obligations under the Columbia Agreement in any material respect and fail to cure such breach in a timely fashion, then Columbia University may terminate the Columbia Agreement. If the Columbia Agreement is terminated, and we lose our intellectual property rights under the Columbia Agreement, this may result in complete termination of our product development and any commercialization efforts for the product candidates that are subject to the agreement, including AT- 007, AT- 001, and AT- 003. While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under the Columbia Agreement, we may not be able to do so in a timely manner, at an acceptable cost or at all. ~~64Furthermore~~ -- **Furthermore** , license agreements we enter into in the future may not provide exclusive rights to use intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. If we are unable to obtain and maintain patent protection for our product candidates and technology, or if the scope of the patent protection obtained is not sufficiently broad or robust, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our product candidates and technology may be adversely affected. Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and our technology. We and our licensors have sought, and intend to seek, to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and our technology that are important to our business. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may

not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by such third- party, or by the U. S. Patent and Trademark Office, or USPTO, itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. The patent prosecution process is expensive, time- consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We or our licensors have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products, if approved. 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 infringing our patents in all countries outside the United States, or from selling or importing products that infringe our patents in and into the United States or other jurisdictions. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if the patent applications we license or own do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. ~~65Furthermore~~ -- **Furthermore**, our owned and in- licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in- licensed patent rights and technology was funded in part by the U. S. government. As a result, the government may have certain rights, or march- in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for noncommercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march- in rights to use or allow third parties to use our licensed technology. The government can exercise its march- in rights if it determines that action is necessary because we fail to achieve practical application of the government- funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U. S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects. Obtaining and maintaining our patent rights depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and / or patent applications will have to be paid to the USPTO and various government patent agencies outside the United States over the lifetime of our owned and licensed patents and / or applications and any patent rights we may own or license in the future. We rely on our service providers or our licensors to pay these fees. The USPTO and various non- U. S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, nonpayment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as or similar to our product candidates, which would have an adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business. In addition, if we fail to apply for applicable patent term extensions or adjustments, we will have a more limited time during which we can enforce our granted patent rights. In addition, if we are responsible for patent prosecution and maintenance of patent rights in- licensed to us, any of the foregoing could expose us to liability to the applicable patent owner. Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. Given the amount of time required for the development, testing and regulatory review of product candidates such as AT- 007, AT- 001, and AT- 003, patents protecting such candidates might expire before or shortly after such candidates are

commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we have or will obtain patent rights. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent; provided that the patent is not enforceable for more than 14 years from the date of drug approval, which is limited to the approved indication (or any additional indications approved during the period of extension). Furthermore, only one patent per approved product can be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. However, the applicable authorities, including the FDA ~~66and~~ -- **and** the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case. Third- parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business. Our commercial success depends, in part, upon our ability and the ability of others with whom we may collaborate to develop, manufacture, market and sell our current and any future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third- party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U. S. patent in federal court, we would need to overcome a presumption of validity. As this is a high burden and requires us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Other companies and research institutions have filed, and may file in the future, patent applications related to AR inhibitors and their therapeutic use. Some of these patent applications have already been allowed or issued, and others may issue in the future. While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third- party patents or patent applications, or we may incorrectly conclude that a third- party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that our product candidate infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from nonpracticing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit. If we are found to infringe a third- party' s valid and enforceable intellectual property rights, we could be required to obtain a license from such third- party to continue developing, manufacturing and marketing our product candidate (s) and technology. Under any such license, we would most likely be required to pay various types of fees, milestones, royalties or other amounts. Moreover, we may not be able to obtain any required license on commercially reasonable terms or at all. The licensing or acquisition of third- party intellectual property rights is a competitive area, and more established companies may also pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license ~~67or~~ **or** acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have an adverse effect on our business, financial condition, results of operations and prospects. Furthermore, even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors and other third- parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. We may be required to indemnify collaborators or contractors against such claims. A finding of infringement could prevent us from manufacturing and commercializing our current or any future product candidates or force us to cease some or all of our business operations, which could harm our business. Even if we are successful in defending against such claims, litigation can be expensive and time- consuming and would divert management' s attention from our core business. 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 an adverse effect on the price of our common stock. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects. We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property. Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s current or former employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self- executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time- consuming and unsuccessful. Competitors may infringe, misappropriate or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time- consuming and are likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may ~~68refuse~~ **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 owned or licensed patents at risk of being invalidated or interpreted narrowly and could put our owned or licensed patent applications at risk of not issuing. The initiation of a claim against a third- party might also cause the third- party to bring counterclaims against us, such as claims asserting that our patent rights are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity 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, non- enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post- grant proceedings such as ex parte reexaminations, inter partes review, post- grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is or will be no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third- party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license, or if the license offered as a result is not on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace. Changes in U. S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current and any future product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the

uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy- Smith America Invents Act, or the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third- party was the first to invent the claimed invention. The America Invents Act also includes a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO- administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or ~~69defense~~ -- **defense** of our issued patents, all of which could have an adverse effect on our business, financial condition, results of operations, and prospects. In addition, the U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. 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 actions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we own, have licensed or might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future. We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business. Filing, prosecuting and defending patents covering our current and any future product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents, and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so 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 intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary 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 and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. 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. Since we rely on third parties to help us discover, develop and manufacture our current and any future product candidates, or if we collaborate with third parties for the development, manufacturing or commercialization of our current or any future product candidates, we must, at times, share trade secrets with them. 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. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar ~~70agreements~~ -- **agreements** with our advisors, employees, third- party contractors 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, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information 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 could have an adverse effect on our business and results of operations. In addition, these agreements typically restrict the ability of our advisors, employees, third- party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know- how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and

we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third- party illegally or unlawfully obtained and is using our trade secrets, like patent litigation, is expensive and time- consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into nondisclosure 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, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, our competitors may independently develop knowledge, methods and know- how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time- consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case ~~71we~~ **we** would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business. We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have selected trademarks for some of our later stage product candidates and filed applications to register those trademarks for our current or any future product candidates. For other earlier stage product candidates, we have not yet selected trademarks or begun the process of applying to register trademarks. Our pending trademark applications, and any future trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks. In addition, any proprietary name we propose to use with our current or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Intellectual property rights do not necessarily address all potential threats to our business. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative: ● others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or license; ● we or our licensors might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license; ● we or our licensors might not have been the first to file patent applications covering certain of our inventions; ● others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; ● it is possible that our pending patent applications will not lead to issued patents; ● issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges; ● our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets; ● we may not develop additional proprietary technologies that are patentable; and ● the patents of others may have an adverse effect on our business. ~~72Risks --~~ **Risks** Related to Our Business Operations, Employee Matters and Managing GrowthWe are ~~highly dependent~~ **involved in a securities- related class action and derivative litigation and defending**

against these claims could result in substantial costs and divert management time and resources, damages and have a material adverse effect on **our results of operations. These lawsuits, and any** ~~the~~ **other** ~~services of~~ **lawsuits to which we are subject, will be costly to defend** ~~our~~ **or pursue and are uncertain in their outcome. The stock markets have from time-to- time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In addition, the market price of our common stock may vary significantly based on specific events, such as receipt of complete response letters, warnings letters, such as the Complete Response Letter and Warning Letter we received from the FDA in November 2024, negative clinical results, a negative vote or decision by an FDA advisory committee, or other negative feedback from the FDA, EMA, or other regulatory agencies. This risk is especially relevant for us because biotechnology and biopharmaceutical companies often experience significant stock price volatility in connection with their investigational drug or medical device product candidate development programs and the regulatory review of their marketing applications. For example, in November 2024, we experienced a significant decline in our stock price based, in large part, on the Complete Response Letter and Warning Letter we received from the FDA. Following receipt of the Complete Response Letter and Warning Letter, a putative class action lawsuit was filed against us and certain of our current and former officers and directors on December 17, 2024, in the United States District Court for the Southern District of New York and is captioned Alexandru v. Applied Therapeutics, Inc., et al., No. 24- cv- 09715. On December 27, 2024, another purported stockholder filed a putative class action lawsuit against us and a former officer and director in the United States District Court for the Southern District of New York (Ikram v. Applied Therapeutics, Inc., et al., No. 1: 24- cv- 09973). On March 11, 2025 the court consolidated the actions (In re Applied Therapeutics Securities Litigation, No. 1: 24- cv- 9715). In addition, on January 31, 2025, certain of our current and former officers and directors were named as defendants in a shareholder derivative action filed in the United States District Court for the Southern District of New York (Hassine v. Shendelman, et al., No. 1: 25- cv- 00935). The complaint seeks to implement reforms to the Company' s corporate governance and internal procedures and to recover on behalf of the Company for any liability the Company might incur as a result of the individual defendants' alleged misconduct, as well as declaratory, equitable, and monetary relief, including attorneys' fees and other costs. The derivative action is based substantially on the same facts alleged in the consolidated action described above. Please refer to " Legal Proceedings " in this Annual Report on Form 10- K for additional information about these pending legal proceedings. The outcome of litigation is necessarily uncertain, and we cannot predict the outcome of these pending legal proceedings. An unfavorable outcome in any such proceeding could have an adverse impact on our business, financial condition, results of operations and cash resources. In addition, we may be exposed to additional litigation or government investigation even if no wrongdoing occurred and we ultimately prevail. Continuing or additional litigation, or responding to any related investigation or enforcement action, as well as a material final judgment or decree against us, would be expensive, divert management' s attention and resources, and could adversely affect our business, financial condition, results of operations and cash resources. Moreover, if our stock price is volatile, we could face additional securities class action lawsuits in the future. We recently experienced the departure of our founder and CEO and changes to our board and our executive management. These changes may create uncertainty and, more generally, if we are unable to attract and retain qualified management, clinical and scientific personnel, our business will be harmed. We have experienced recent changes to our senior management team and board, including the departures of our founder, President,** Chief Executive Officer **, Secretary** and ~~Chairman~~ **member of the board** , Dr. Shoshana Shendelman, **on December 19, 2024,** and **member of the board, Joel Marcus, on December 6, 2024. Les Funtleyder,** our Chief ~~Medical~~ **Financial** Officer, **is serving as Interim** ~~Dr. Riccardo Perfetti, and if we are not able to retain these members of our management team or recruit and retain additional management, clinical and scientific personnel, our business will be harmed. We are highly dependent on our~~ Chief Executive Officer ~~and~~ **while our board conducts a search for a permanent Chief Executive Officer. On December 19, 2024, our board also appointed John H. Johnson as Executive** Chairman ~~, Dr. Shoshana Shendelman,~~ and **as Chairman** ~~our Chief Medical Officer, Dr. Riccardo Perfetti. Each~~ of ~~them~~ **the Board. Changes in our board and senior management and uncertainty regarding pending changes** may ~~currently terminate~~ **disrupt our business and investor relationships, and impair our ability to recruit and retain** ~~their~~ **other needed** ~~employment with us at any time. The loss of the services of either of these persons~~ **personnel . Any such disruption or impairment** could **have** ~~impede the achievement of our research, development and~~ **an** ~~commercialization objectives~~ **adverse effect on our business** . Recruiting and retaining other senior executives, qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high- quality personnel, our ability to pursue our growth strategy will be limited. Our future performance will also depend, in part, on our ability to successfully integrate

newly hired executive officers into our management team **, including Mr. Johnson,** and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. Additionally, we do not currently maintain " key person " life insurance on the lives of our executives or any of our employees. ~~We expect~~ **If we determine** to ~~expand our organization,~~ **bring in- house some functions that we are currently outsourcing** and **if we commercialize any of our product candidates** we may experience difficulties in managing this growth, which could disrupt our operations. As of December 31, ~~2023~~ **2024** , we had ~~25~~ **35** full- time employees. As the clinical development of our product candidates progresses, we also expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. ~~73Our~~ -- **Our** internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively, and adversely affect our business and operating results. Our internal computer systems, cloud- based computing services and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage or interruption from computer viruses, data corruption, cyber- based attacks (including phishing attempts, denial of service attacks, and malware or ransomware incidents **, attacks enhanced or facilitated by artificial intelligence**), unauthorized access, natural disasters, terrorism, war, international hostilities and telecommunication and electrical failures. While we have not experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, federal, state and international laws and regulations, such as the European Union' s General Data Protection Regulation, which took effect in May 2018, can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties and significant legal liability, if our information technology security efforts fail. In addition, our software systems include cloud- based applications that are hosted by third- party service providers with security and information technology systems subject to similar risks. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. Risks of unauthorized access and cyber- attacks have increased as most of our personnel, and the personnel of many third- parties with which we do business, have adopted remote working arrangements as a result of the ~~Covid~~ **COVID** - 19 pandemic, and may increase as a result of recent hostilities between Russia and Ukraine. Improper or inadvertent employee behavior, including data privacy breaches by employees, contractors and others with permitted access to our systems, may also pose a risk that sensitive data may be exposed to unauthorized persons or to the public. If a system failure or security breach occurs and interrupts our operations or the operations at one of our third- party vendors, it could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber- attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and / or our financial information and adversely affect our business or reputation or result in legal or regulatory proceedings. In addition, if a ransomware attack or other cyber- attack occurs, either internally or at our third- party vendors, we could be prevented from accessing our systems or data, which may cause interruptions or delays in our business, cause us to incur remediation costs or subject us to demands to pay ransom, or adversely affect our business reputation **. Additionally, the increased prevalence and use of artificial intelligence may heighten the risk that we may be subject to cybersecurity incidents in the future. Although we don' t currently rely on or use artificial intelligence in our operations, if any of our third- party vendors who use artificial intelligence are compromised, it could have a negative impact to our business through leaks of our confidential information and / or our financial information and adversely affect our business or reputation or result in legal or regulatory proceedings** . Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance 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 FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, 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 restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of ~~74clinical~~ -- **clinical** trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government 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 result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government- funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects. Any future acquisitions or strategic collaborations may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and / or subject us to other risks. From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic partnership may entail numerous risks, including: ● ● increased operating expenses and cash requirements; ● ● the assumption of additional indebtedness or contingent or unknown liabilities; ● ● assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel; ● ● the diversion of our management' s attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition; ● ● retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships; ● ● risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or product candidates and regulatory approvals; and ● ● our inability to generate revenue from acquired technology and / or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs. In addition, if we engage in future acquisitions or strategic partnerships, we may issue dilutive securities, assume or incur debt obligations, incur large one- time expenses, and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or drugs that may be important to the development of our business ~~. We have identified a material weakness in our internal control over financial reporting during the year ended December 31, 2023 related to deficiencies in our controls over the financial statement close process. If we are unable to maintain an effective system of disclosure controls and procedures and internal control over financial reporting, we may not be able to accurately report our financial results in a timely manner, which may adversely affect investor confidence in us and materially and adversely affect our business and financial results. In connection with our audit as of and for the period ended December 31, 2023, we identified a material weakness in our internal control over financial reporting relating to deficiencies in our controls over the financial statement close process. Specifically, there were deficiencies in the design and operation of internal controls over the review of complex accounting issues involving significant judgment or estimates with respect to certain transactions. See " Item 9A. Controls and Procedures " for more information. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Effective internal controls are necessary for us to provide 75reliable financial reports and prevent fraud. We have and continue to take steps to remediate the material weakness, but there is no assurance that any remediation efforts will ultimately have the intended effects. If we identify any new material weaknesses in the future, any such newly identified material weakness could limit our ability to prevent or detect a misstatement of our accounts or disclosures that could result in a material misstatement of our annual or interim financial statements. In such case, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We cannot assure stockholders that the measures we have taken to date, or any measures we may take in the future, will be sufficient to avoid potential future material weaknesses~~ . Risks Related to Ownership of Our Common StockThe market price of our common stock is volatile and has fluctuated substantially, which could result in substantial losses for purchasers of our common stock. The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which you purchased it. In addition to the factors discussed in this " Risk Factors " section and elsewhere in this Annual Report, the market price for our common stock has been, and is likely to continue to be influenced by the following: ● ● the commencement, enrollment, results of, or any delays in our planned or future clinical trials of our product candidates or those of our competitors; ● ● the success of competitive drugs or therapies; ● ● **the Complete Response Letter we received from the FDA for the NDA we submitted for govorestat; • the departure of our founder and CEO and changes to our senior management team and board; •** regulatory or legal developments in the United States and other countries; ● ● the success of competitive products or technologies; ● ● developments or disputes concerning patent applications, issued patents or other proprietary rights; ● ● the recruitment or departure of key personnel; ● ● the level of expenses related to our product candidates or clinical development programs; ● ● the results of our efforts to discover, develop, acquire or in- license additional product candidates; ● ● actual or anticipated changes

in estimates as to financial results, development timelines or recommendations by securities analysts; ● our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices; ● disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; ● significant lawsuits, including patent or stockholder litigation; ● variations in our financial results or those of companies that are perceived to be similar to us; ● changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug; ● market conditions in the pharmaceutical and biotechnology sectors; ● general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad; and ● investors' general perception of us and our business. These and other market and industry factors have caused the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common stock. Furthermore, we believe our stock has been, and may in the future be, adversely affected as a result of actions by third- parties. Short sellers and others, some of whom post anonymously on social media, may be positioned to profit if our stock declines and their activities can negatively affect our stock price. ~~76Some --~~ **Some** companies that have experienced volatility in the trading price of their shares have been the subject of **lawsuits and / or** securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time- consuming, and could divert our management' s attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common stock. ~~Concentration~~ **If we fail to regain compliance with the continued listing requirements** of ~~ownership of~~ **Nasdaq,** our common stock ~~among our existing executive officers, directors and principal stockholders~~ may **be delisted and the price** ~~prevent new investors from influencing significant corporate decisions. Based upon shares~~ of our common stock ~~outstanding as of December 31~~ **and our ability to access the capital markets could be negatively impacted. On February 7** , ~~2023~~ **2025** , **we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market,** ~~our --~~ **or Nasdaq** ~~executive officers~~ , **notifying us** ~~directors and stockholders who owned more than~~ **that** ~~10 % of~~ **, for the last 30 consecutive business days, the bid price for** our ~~outstanding~~ common stock ~~, in~~ **had closed below** the ~~aggregate, beneficially own~~ **minimum $ 1. 00 per** ~~shares --~~ **share** ~~representing approximately 26~~ **requirement for continued inclusion on the Nasdaq Global Market, referred to as the minimum bid price rule** . ~~5 %~~ **In accordance with Nasdaq Listing Rules, we have an initial period** of **180 calendar days,** ~~our --~~ **or** ~~outstanding~~ **until August 6, 2025, to regain compliance with the minimum bid price rule. If at any time before August 6, 2025 the bid price for our** common stock **closes at $ 1. 00 or more per share for a minimum of 10 consecutive business days, the Nasdaq Listing Qualifications Department staff will provide written notification to us that we are in compliance with the minimum bid price rule, unless the staff exercises its discretion to extend this 10- day period pursuant to the Nasdaq Listing Rules** . If ~~our executive officers~~ **we do not regain compliance with the minimum bid price rule by August 6** , ~~directors~~ **2025, we may be eligible for** ~~and --~~ **an additional** ~~stockholders who owned more than 10~~ **180 % calendar day compliance period. We intend to monitor the closing bid price** of our ~~outstanding~~ common stock ~~acted together~~ **and may** , **if appropriate, consider available options to regain compliance with** ~~they --~~ **the minimum bid price rule. There are** ~~may~~ **many factors that may adversely affect our minimum bid price, including those described throughout this section titled " Risk Factors. " Many of these factors are outside of our control. As a result, we may not** be able to **sustain compliance with** ~~significantly influence all matters requiring stockholder approval, including~~ the **minimum bid price rule in the long** ~~election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms --~~ **term** ~~that~~ **. Any potential delisting of our common stock from** ~~other --~~ **the Nasdaq Global Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Global Market would also make it more difficult for our** stockholders ~~may desire~~ **to sell** ~~or~~ **our result** **common stock** in ~~the management of our company in ways with which other --~~ **the** ~~stockholders disagree~~ **public market** . Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. You should not rely on an investment in our common stock to provide dividend income. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock. Future sales of common stock by holders of our common stock, or the perception that such sales may occur, could depress the market price of our common stock. Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, ~~2023~~ **2024** , we had outstanding ~~84~~ **137** , ~~869~~ **228** , ~~832~~ **741** shares of common stock. A substantial number of such shares are currently restricted as a result of securities laws or lock- up agreements but will be able to be sold in the future. We further have registered all shares of common stock that we may issue in the future or have issued to date under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and certain lock- up agreements. Sales of a large number of the shares issued under these plans in the public market could have an adverse effect on the market price of our common stock. General Risk ~~FactorsIf --~~ **Factors If** research analysts do not publish research or reports, or publish unfavorable

research or reports, about us, our business or our market, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that industry or financial analysts publish about us or our business. Equity research analysts may discontinue research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research ~~77about~~ -- **about** us. If one or more equity research analysts cease coverage of us or fail to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common stock to decline. We have broad discretion in the use of our cash and cash equivalents and may use them ineffectively, in ways with which you do not agree or in ways that do not increase the value of your investment. Our management has broad discretion in the application of our cash and cash equivalents, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in additional operating losses that could have a negative impact on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value. We ~~are~~ **no longer qualify as** an " emerging growth company, " and ~~the reduced~~ **as a result, we have to comply with increased** disclosure **and compliance** requirements ~~applicable to emerging growth~~ **. While we still qualify as a " smaller reporting** ~~companies~~ **company** ~~may make our common stock less attractive to investors. We are~~ **, " as defined in Regulation S- K of the Securities Act of 1933, we no longer qualify as** an "~~-~~emerging growth company ~~,~~ **(" EGC** " **)** ~~or EGC,~~ as defined in the Jumpstart Our Business Startups Act ~~of~~ **because in** ~~2012~~ - **2024** , **we reached the five- year anniversary of the first sale of** ~~or~~ **our common stock pursuant to an effective registration statement under** the ~~JOBS~~ **Securities** Act ~~, and we intend to take advantage~~ of ~~some of the~~ **1933. As such, we are no longer** ~~exemptions~~ ---- **exempt** from ~~reporting~~ **certain disclosure and compliance** requirements that **apply** ~~are applicable~~ to other public companies ~~that~~ **but did not previously apply to us due to our status as an EGC. These requirements include, but** are not **limited to** ~~EGCs, including~~ : **• compliance** ~~● being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced " Management' s Discussion and Analysis of Financial Condition and Results of Operations " disclosure; ● not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting; ● not being required to comply~~ with any requirement that may be adopted by the **PCAOB** ~~Public Company Accounting Oversight Board~~ regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements **, including critical audit matters** ; ~~● reduced~~ **• the requirement that we provide more detailed** ~~disclosure~~ **disclosures** ~~obligations~~ regarding executive compensation **, although we are still able to take advantage of exemptions provided to smaller reporting companies** ; and **• the requirement that we obtain** ~~● not being required to hold a nonbinding advisory vote on executive compensation and~~ stockholder approval of any golden parachute payments not previously approved. We ~~cannot predict whether~~ **anticipate increased expenses, including exchange listing and SEC requirements, director and officer insurance premiums, legal, audit and tax fees, regulatory compliance programs, and** ~~investors~~ -- **investor relations costs associated with being** ~~will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as~~ a ~~result, there may~~ **public company and ceasing to** be ~~a less active trading market for our common stock and~~ - **an emerging growth company** ~~our share price may be more volatile~~ . We ~~currently take advantage of some or all of these reporting exemptions until we are no longer an EGC. We will remain an EGC until the earlier of (i) December 31, 2024, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least $ 1. 235 billion, (iii) the last day of the first fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non- affiliates exceeds $ 700 million as of the prior June 30th, and (iv) the date on which we have issued more than $ 1. 0 billion in non- convertible debt during the prior three- year period. Even after we no longer qualify as an EGC, we may still qualify as a " smaller reporting company " or " non- accelerated filer, " which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, under Section 107 (b) of the JOBS Act, EGCs can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not EGCs. 78We~~ have incurred increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives. As a public company, and particularly ~~after~~ **now that** we are no longer an EGC, we incur and will continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes- Oxley Act of 2002, or the Sarbanes- Oxley Act, and rules subsequently implemented by the SEC and The Nasdaq Stock Market LLC have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to comply with these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time- consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance. Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and

challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions: • establish a classified board of directors such that not all members of the board are elected at one time; • allow the authorized number of our directors to be changed only by resolution of our board of directors; • limit the manner in which stockholders can remove directors from the board; • establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors; • require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent; • limit who may call stockholder meetings; • authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so- called " poison pill, " that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and • require the approval of the holders of at least 662 / 3 % of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws. ~~79~~ **Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock. Our governing documents designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that, with respect to any state actions or proceedings under Delaware statutory or common law, the Court of Chancery of the State of Delaware is the exclusive forum for: • any derivative action or proceeding brought on our behalf; • any action asserting a breach of fiduciary duty; • any action asserting a claim against us or any of our directors, officers, employees or agents arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; • any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; and • any action asserting a claim against us or any of our directors, officers, employees or agents that is governed by the internal- affairs doctrine. In addition, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States are, to the fullest extent permitted by law, the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These exclusive- forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find an exclusive- forum provision in our amended and restated certificate of incorporation or our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could harm our business.**