Risk Factors Comparison 2025-02-27 to 2024-02-29 Form: 10-K

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The following summarizes the principal factors that make an investment in the Company speculative or risky, all of which are more fully described in the Risk Factors section below. This summary should be read in conjunction with the Risk Factors section and should not be relied upon as an exhaustive summary of the material risks facing our business. The occurrence of any of these risks, could harm our business, financial condition, results of operations and / or growth prospects or cause our actual results to differ materially from those contained in forward- looking statements we have made in this Annual Report on Form 10- K and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business. Risk Factor Summary Risks Related to Our Financial Condition and Capital Requirements • We will not be able to continue as a going concern if we are unable to raise additional capital when needed **and raising additional capital may cause dilution to our stockholders and restrict our operations** . • We have never generated any revenue from product sales and may never be profitable. • We anticipate that we will continue to incur significant losses for the foreseeable future. ~~• We may not be able to raise the capital that we need to support our business plans and raising additional capital may cause dilution to our stockholders and restrict our operations.~~ Risks Related to ~~the~~ Discovery, Development and Commercialization ~~• We face competition from companies that have developed or may develop competing programs.~~ • Our programs are in ~~preclinical~~ --- **clinical and nonclinical** stages of development and may fail ~~in development~~ or suffer delays **or may be more costly than anticipated for various reasons, including but not limited to delays or failures in achieving alignment with regulatory authorities on trial designs and interpretation of data and its sufficiency to support safety and efficacy of our product candidates, patient recruitment or other clinical trial challenges, or unanticipated drug supply disruptions** . • We are substantially dependent on the success of the SPY001 ~~and~~ **,** SPY002 **and SPY003** programs ~~. • We~~ **, alone or in combination, and** may fail to achieve our projected development goals in the time frames we ~~announce and~~ expect. • Any drug delivery device ~~potentially~~ used may have its own regulatory development, supply, and other risks. • We may not be successful in ~~our efforts to build~~ **building** a pipeline of product candidates with commercial value. • Our studies and trials may ~~not~~ be ~~sufficient~~ **insufficient** to support regulatory approval of any ~~of our~~ product candidates. • **We** ~~If we are unable to successfully develop complementary diagnostics for our therapeutic product candidates, we~~ may not **be successful** ~~realize their full commercial potential. • We have limited experience~~ in **discovering,** developing and commercializing ~~diagnostics and have never applied for or~~ **our intraportfolio investigational drug** ~~obtained regulatory clearance or approval for any diagnostic tests. • Additional time may be required to obtain regulatory approval for our product candidates and future product candidates because of their status as combination~~ **combinations to achieve superior outcomes relative to the use of other therapies** ~~products. • We may encounter difficulties enrolling participants in our future clinical trials~~ . • Preliminary or " topline " data from our clinical trials may change as more data becomes available. • Our **current or** future clinical trials may reveal significant adverse events or **undesirable** side effects. • We may fail to capitalize on more profitable or potentially successful product candidates ~~than those we pursue~~ . • **Our** ~~Any of our future approved~~ products may not achieve regulatory approval, market acceptance or commercial success. • **Our** ~~Certain of our~~ programs may compete with ~~our~~ **each** other **and they face third- party** ~~programs~~ **program competition** . • The FDA may not accept data from clinical trials we conduct at sites outside the United States. Risks Related to Government Regulation • **We** ~~FDA and comparable foreign regulatory approval processes are lengthy and time- consuming and we~~ may not be able to **achieve our timelines or** obtain **timely** ~~, or may be delayed in obtaining,~~ regulatory approvals **of** ~~for our~~ product candidates. • We may not be able to meet requirements for chemistry, manufacturing and control of our programs. • Our product candidates may face competition sooner than anticipated based on rules and regulations that may apply or government decisions with respect to our intellectual property. • Even if we receive regulatory approval, we will be subject to extensive ongoing regulatory obligations. • We may face difficulties from healthcare **and other** legislative reform measures **and other changes in law** . • Our **potential revenue** ~~operations and arrangements with third- parties are subject to healthcare regulatory laws. • We~~ may be **adversely affected** ~~unable to offer products at competitive prices~~ due to unfavorable ~~pricing~~ regulations and / or ~~third- party coverage and reimbursement~~ policies. • We may face criminal liability or other consequences ~~for violations of~~ **if we violate** U. S. and foreign trade regulations ~~. • Foreign governments may impose strict price controls, which may adversely affect our revenue~~ . • Any accelerated review designations ~~(e. g. fast track designation)~~ we may pursue may not hasten development or regulatory review. Risks Related to Our Intellectual Property • ~~Our ability to~~ **We may fail in** ~~obtain~~ **obtaining , maintaining** and ~~protect~~ **protecting** our patents and other proprietary rights ~~is uncertain. • We may fail in obtaining or maintaining necessary rights to our programs~~ . • We may be subject to patent infringement claims or may need to file such claims. • We may be subject to claims of wrongful hiring of employees or wrongful use of confidential information. • Our patents and our ability to protect our products may be impaired by changes to patent laws. • Our patent protection could be reduced or eliminated for non- compliance with ~~regulatory~~ **legal** requirements. • We may fail to identify or interpret relevant third- party patents. • We may become subject to claims challenging the inventorship or ownership of our intellectual property. • Patent terms may be inadequate to protect our competitive position of our programs. • Our technology licensed from various third parties may be subject to retained rights. Risks Related to Our Reliance on Third Parties • We may fail to maintain collaborations and licensing arrangements with third parties that we rely on. • Third ~~-~~ parties we rely on for **nonclinical** ~~the execution of preclinical~~ studies and clinical trials may fail to **satisfy** ~~carry out their~~ contractual duties. • We may be unable to use third- party manufacturing sites ~~or~~ **,** our third- party manufacturers may encounter difficulties in production **or we may need to switch or create third- party manufacturer redundancies** . Risks Related to Employee Matters, Managing

Growth and Other Risks Related to Our Business • We may experience difficulties in managing the growth of our organization. • We may fail to attract or retain highly qualified personnel. • Our ability to operate in foreign markets is subject to regulatory burdens, risks and uncertainties. • Our estimates of market opportunity ~~and forecasts of market growth~~ may be inaccurate and our business may not grow at similar rates ~~, or at all~~ . • Our employees or third ~~-~~ parties may engage in misconduct or other improper activities. • We may be impacted by security or data breaches or other improper access to our data. • Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. • We may fail to comply with privacy ~~and~~ **,** data security **, safety and other** regulations **despite compliance efforts** ~~. • We may fail to comply with environmental, health and safety laws and regulations~~ . • We may be subject to adverse legislative or regulatory tax changes. • We may fail to realize the benefits of our business or product acquisitions or our strategic alliances ~~. • We may be impacted by the failure of financial institutions~~ . Risks Related to Our Common Stock • **The market price** ~~We may fail to obtain stockholder approval~~ of ~~the conversion of~~ our **common** ~~Series B Preferred Stock~~ **stock has historically been volatile and may drop in the future** . • Our certificate of incorporation, Delaware law and certain contracts include anti- takeover ~~provisions. • Our certificate of incorporation and bylaws contain exclusive forum~~ provisions. • We do not anticipate paying any dividends in the foreseeable future. • Future sales **and issuances** of ~~shares by existing~~ **equity / debt may dilute** stockholders ~~could cause~~ **and / or result in a drop in** our stock price ~~to decline. • Future sales and issuances of equity and debt could result in additional dilution to our stockholders~~ . • Our principal stockholders own a significant percentage of our stock. General Risk Factors • **Our product liability insurance** ~~The market price of our common stock has historically been volatile and~~ may ~~drop in~~ **be insufficient to cover costly and damaging liability claims. • Litigation costs and** the ~~future~~ **outcome of litigation could have a material adverse effect on our business** . • We **continue to** incur significant costs **for compliance** ~~associated with complying~~ with public company **laws and regulations** ~~reporting requirements. • A lack of analyst coverage may cause a decline in our stock price or trading volume~~ . • We may fail to maintain proper and effective internal controls **. We have identified a material weakness in our internal control over financial reporting over financial reporting which could, if not remediated, adversely affect our ability to report our financial condition and results of operations in a timely and accurate manner, decrease investor confidence in us, and reduce the value of our common stock. • Our business could be adversely affected by macroeconomic conditions** . We will need to raise additional capital, and if we are unable to do so when needed, we will not be able to continue as a going concern. ~~This Annual Report includes disclosures regarding our management' s assessment of our ability to continue as a going concern.~~ As of December 31, ~~2023~~ **2024** , we had $ ~~339~~ **603** . ~~6~~ **1** million of cash, cash equivalents, **and** marketable securities ~~, and restricted cash~~ . We will need to raise additional capital to continue to fund our operations ~~and service our debt obligations~~ in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern. Developing our product candidates requires a substantial amount of capital. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we advance our product candidates through clinical trials. We will need to raise additional capital to fund our operations and such funding may not be available to us on acceptable terms, or at all, and such funding may become even more difficult to obtain due to rising interest rates and ~~the current downturn~~ **downturns** in the U. S. capital markets and the biotechnology sector in general. Competition for additional capital among biotechnology companies may be particularly intense during ~~this present~~ economic ~~downturn~~ **downturns** . We may be unable to raise capital through public offerings of our common stock and may need to turn to alternative financing arrangements. Such arrangements, if we pursue them, could involve issuances of one or more types of securities, including common stock, ~~Preferred~~ **preferred** ~~Stock~~ **stock** , convertible debt, warrants to acquire common stock or other securities. These securities could be issued at or below the then prevailing market price for our common stock. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make- whole has been paid. Interest on any newly- issued debt securities and / or newly- incurred borrowings would increase our operating costs and reduce our net income (or increase our net loss), and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be materially and adversely affected. We do not currently have any products approved for sale and do not generate any revenue from product sales. Accordingly, we expect to rely primarily on equity and / or debt financings to fund our continued operations. Our ability to raise additional funds will depend, in part, on the success of our ~~preclinical~~ **nonclinical** studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to: • significantly delay, scale back, or discontinue the development or commercialization of our product candidates; • seek strategic partnerships, or amend existing partnerships, for research and development programs at an earlier stage than otherwise would be desirable or that we otherwise would have sought to develop independently, or on terms that are less favorable than might otherwise be available in the future; • dispose of technology assets, or relinquish or license on unfavorable terms, our rights to technologies or any of our product candidates that we otherwise would seek to develop or commercialize ourselves; • pursue the sale of our company to a third party at a price that may result in a loss on investment for our stockholders; or • file for bankruptcy or cease operations altogether (and face any related legal proceedings). Any of these events could have a material adverse effect on our business, operating results and prospects. Even if successful in raising new capital, we could be limited in the amount of capital we raise due to investor demand restrictions placed on the amount of capital we raise or other reasons. Additionally, any capital raising efforts are subject to significant risks and contingencies, as described in more detail under the risk factor titled " Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights. " We have no products approved for commercialization and have never generated any revenue from product

sales. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to: • completing research and development of our product candidates; • obtaining regulatory and marketing approvals for our product candidates for which we complete clinical trials; • manufacturing product candidates and establishing and maintaining supply and manufacturing relationships with third parties that are commercially feasible, meet regulatory requirements and our supply needs in sufficient quantities to meet market demand for our product candidates, if approved; • qualify for adequate coverage and reimbursement by government and third- party payors for any product candidates for which we obtain regulatory and marketing approval; • marketing, launching, and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor; • gaining market acceptance of our product candidates as treatment options; • addressing any competing products and technological and market developments; • implementing internal systems and infrastructure, as needed; • protecting and enforcing our intellectual property rights, including patents, trade secrets, and know- how; • negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter; • obtaining coverage and adequate reimbursement from third- party payors and maintaining pricing for our product candidates that supports profitability; and • attracting, hiring, and retaining qualified personnel. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by regulatory authorities to perform clinical and other studies in addition to those that we anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Portions of the research programs with respect to which we have **signed a license agreement,** exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement may be in- licensed from third parties, which make the commercial sale of such in- licensed products potentially subject to additional royalty and milestone payments to such third parties. We will also have to develop or acquire manufacturing capabilities or continue to contract with contract manufacturers in order to continue development and potential commercialization of our product candidates. For instance, if the costs of manufacturing our drug product are not commercially feasible, we will need to develop or procure our drug product in a commercially feasible manner in order to successfully commercialize a future approved product, if any. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable. We have historically incurred losses, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future. We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. For the years ended December 31, **2024,** 2023 ~~,~~ **and** 2022 ~~and 2021~~, we reported a net loss of $ **208. 0 million, $** 338. 8 million ~~,~~ **and** $ 83. 8 million ~~and $ 65. 8 million~~, respectively. As of December 31, ~~2023~~ **2024**, we had an accumulated deficit of $ ~~764~~ **972**. 4 million. We will need to raise substantial additional capital to continue to fund our operations in the future ~~. If our stockholders do not timely approve the conversion of our Series B Preferred Stock, then the holders of our Series B Preferred Stock may be entitled to require us to settle their shares of Series B Preferred Stock for cash at a price per underlying share of common stock equal to the last reported closing sale price of common stock on the principal trading market on which the common stock is listed as of the trading day immediately prior to the date on which a request to convert shares of Series B Preferred Stock into shares of common stock is delivered to us by a holder in accordance with the terms of the Series B Certificate of Designation and we fail to deliver such shares of common stock, as described in our Series B Certificate of Designation relating to the Series B Preferred Stock. Because the specific timing of the exercise of the cash redemption is not under our control and is dependent the closing sale price of our common stock at the time of such conversion, we cannot quantify the aggregate amount of the potential cash settlement; however, for illustrative purposes only, if all of our holders of Series B Preferred Stock had delivered requests to convert their shares of Series B Preferred Stock on February 26, 2024 and assuming we were obligated to settle such conversions in cash pursuant to the terms of the Series B Certificate of Designation, a total of $ 141, 480, 000 would have been payable to such holders as a result of the cash settlement of all 6, 000, 000 shares of common stock issuable upon the conversion of 150, 000 shares of Series B Preferred Stock, at a price of $ 23. 58 per share of common stock, which was the closing sale price of our common stock on the Nasdaq Global Select Market on February 23, 2024~~. Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on our financial condition and our ability to develop our product candidates. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. If we are unable to acquire additional capital or resources, we will be required to modify our operational plans to complete future milestones and we may be required to delay, limit, reduce or eliminate development or future commercialization efforts of product candidates and / or programs. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate. We may be forced to reduce our operating expenses and raise additional funds to meet our working capital needs, principally through the additional sales of our securities or debt financings or entering into strategic collaborations. We have devoted substantially all of our financial resources to identify, acquire, and develop our product candidates, including conducting ~~preclinical~~ **nonclinical** and clinical development of the legacy rare disease clinical ~~studies~~ **trials** conducted by us prior to the Asset Acquisition ~~(the" Legacy Pipeline")~~ and the **nonclinical and** ~~preclinical~~ --- **clinical** development of our current ~~IBD~~ pipeline, and providing general and administrative support for our operations. To date, we have funded our operations primarily from the sale and issuance of convertible preferred and common equity securities, pre- funded warrants, the collection of grant proceeds, and the licensing of our product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. The amount of our future net losses will depend, in part, on the rate of our future

expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We expect our losses to increase as our product candidates enter more advanced clinical trials. It may be several years, if ever, before we complete pivotal clinical trials or have a product candidate approved for commercialization. We expect to invest significant funds into the research and development of our current product candidates to determine the potential to advance these product candidates to regulatory approval. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, coverage and adequate reimbursement from third- party payors, and adequate market share for our product candidates in those markets. Even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval could be very small, we may never become profitable despite obtaining such market share and acceptance of our products. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future and our expenses will increase substantially if and as we: • continue the **nonclinical** ~~preclinical development~~ and ~~initiate the~~ clinical development of our product candidates; • continue efforts to discover and develop new product candidates; • continue the manufacturing of our product candidates or increase volumes manufactured by third parties; • advance our product candidates into larger, more expensive clinical trials; • initiate additional ~~preclinical~~ **nonclinical** studies or clinical trials for our product candidates; • seek regulatory and marketing approvals and reimbursement for our product candidates; • establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval and market for ourselves; • seek to identify, assess, acquire, and / or develop other product candidates; • make milestone, royalty, or other payments under third- party license agreements; • seek to maintain, protect, and expand our intellectual property portfolio; • ~~pay penalties under our registration rights agreement for failing to timely register the applicable securities; •~~ seek to attract and retain skilled personnel; and • experience any delays or encounter issues with the development and potential for regulatory approval of our clinical and product candidates such as safety issues, manufacturing delays, clinical trial accrual delays, longer follow- up for planned studies or trials, additional major studies or trials, or supportive trials necessary to support marketing approval. Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. Until such time, if ever, as we can generate substantial revenue from the sale of our product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements. To the extent that we raise additional capital through the sale of equity securities or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements with third parties when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves. To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in December 2023, we sold an aggregate of 6, 000, 000 shares of **our** common stock and 150, 000 shares of our Series B Preferred Stock **pursuant** ~~in the December 2023 PIPE~~ to ~~the December 2023~~ **a private placement to certain** ~~Investors~~ **investors** for gross proceeds of **approximately** $ 180 ~~. 0~~ million **and in March 2024, we sold an aggregate of 121, 625 shares of our Series B Preferred Stock pursuant to a private placement to certain investors for gross proceeds of approximately $ 180 million** . Subject to ~~receiving the requisite stockholder approval and~~ certain beneficial ownership limitations set by each holder of Series B Preferred Stock, each share of Series B Preferred Stock **is** ~~will automatically convert~~ **convertible** into an aggregate of 40 shares of our common stock. **Following** ~~We are required to solicit the consent of our stockholders~~ - **stockholder** ~~with regard to~~ **approval of the Series B** ~~conversion~~ **Conversion** ~~of the~~ **Proposal, 254, 958** shares of ~~our~~ Series B Preferred Stock **automatically converted** ~~which will be voted on at our 2024 annual meeting of stockholders. If our stockholders fail~~ to **10** ~~approve such matters~~ , **198** ~~we may be subject to financial penalties that could materially harm our business~~ , **320 shares** ~~including the forced settlement~~ of **common stock; 16, 667** shares of Series B Preferred Stock ~~for cash,~~ **did not automatically convert and remain outstanding** as ~~described in our Series B Certificate~~ of ~~Designation~~ **December 31, 2024 due to beneficial ownership limitations** . Debt financing, if available, would likely involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, making additional product acquisitions, or declaring dividends. If we raise additional funds through strategic collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates or future revenue streams or grant licenses on terms that are not favorable to us. We cannot be assured that we will be able to obtain additional funding if and when necessary to fund our entire portfolio of product candidates to meet our projected plans. If we are unable to obtain funding on a timely basis, we may be required to delay or discontinue one or more of our development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on potential business opportunities, which could materially harm our business, financial condition, and results of operations. ~~Risks Related to Discovery, Development and Commercialization~~ We face competition from entities that have developed or may develop programs for the diseases addressed by our product candidates. The development and

commercialization of drugs is highly competitive. Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies and emerging biotechnology companies, as well as academic institutions, governmental agencies, and public and private research institutions, among others. Many of the companies with which we are currently competing or will ~~complete~~ **compete** against in the future have significantly greater financial resources and expertise in research and development, manufacturing, ~~preclinical~~ **nonclinical** testing, clinical trial conduct, regulatory approvals, and marketing than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, recruiting participants for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our product candidates. Our competitors have developed, are developing or will develop programs and processes competitive with our programs and processes. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments. Our success will depend partially on our ability to develop and commercialize products that have a competitive safety, efficacy, dosing and / or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance. See the section titled " Business – Competition " **in this Annual Report on Form 10- K** for more discussion about our competitors. In addition, because of the competitive landscape for inflammatory and immunology (" I & I") indications, we may also face competition for clinical trial enrollment. Clinical trial enrollment will depend on many factors, including if potential clinical trial participants choose to undergo treatment with approved products or enroll in competitors' ongoing clinical trials for programs that are under development for the same indications as our programs. An increase in the number of approved products for the indications we are targeting with our programs may further exacerbate this competition. Our inability to enroll a sufficient number of participants could, among other things, delay our development timeline, which may further harm our competitive position. Our product candidates are in ~~preclinical~~ --- **clinical and nonclinical** stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our current or future collaborators are unable to complete development of, or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed. We have no products on the market ~~,~~ and all of our product candidates are in ~~preclinical~~ --- **clinical or nonclinical** stages of development **,** and **we** have not ~~been tested in humans~~ **completed any clinical trials** . As a result, we expect it will be many years before we commercialize any product candidate, if ever. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for, and successfully commercializing, our product candidates, either alone or with third parties, and we cannot guarantee ~~you~~ that we will ever obtain regulatory approval for any of our product candidates. We have not yet demonstrated our ability to ~~initiate or~~ complete any clinical trials, obtain regulatory approvals, manufacture a ~~clinical or~~ commercial **-** scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or an existing or future collaborator must conduct extensive ~~preclinical~~ **nonclinical** tests and clinical trials to demonstrate the safety and efficacy in humans of our programs and future product candidates. We or our collaborators may experience delays in initiating or completing **nonclinical studies or** clinical trials. We or our collaborators also may experience numerous unforeseen events during, or as a result of, any current or future **nonclinical studies and** clinical trials that we could conduct that could delay or prevent our ability to **achieve our development timelines,** receive marketing approval or commercialize our current product candidates or any future product candidates, including: • regulators **, such as the FDA,** or **ethics committees (" ECs ") /** institutional review boards (" IRBs ") ~~, the FDA or ethics committees~~ may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations (" CROs "), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • clinical trial sites **may** ~~deviating~~ **deviate** from trial protocol or ~~dropping~~ **drop** out of a trial; • clinical trials of any product candidates may fail to ~~show~~ **demonstrate** safety or efficacy, **or** produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional ~~preclinical~~ **nonclinical** studies or clinical trials **,** or we may decide to abandon product development programs; • the number of ~~subjects~~ **participants** required for clinical trials of any product candidates may be larger than we anticipate **and** ~~, especially if regulatory bodies require completion of non- inferiority or superiority trials,~~ enrollment in these clinical trials may be slower than we anticipate or ~~subjects~~ **participants** may drop out of these clinical trials or fail to return for post- treatment follow- up at a higher rate than we anticipate; • our third- party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators; • we may elect to, or regulators ~~,~~ **and / or ECs /** IRBs ~~or ethics committees~~ may require that we or our investigators **materially modify** , suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks; • the cost of clinical trials of any of our programs may be greater than we anticipate; • the quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial; • ~~our inability~~ **we may be unable** to manufacture sufficient quantities of our product candidates for use in clinical trials; • reports from clinical testing of other therapies may raise safety or efficacy concerns about our programs; • **the FDA** ~~our~~ **or** ~~failure~~ **other regulatory authorities may not agree with our interpretation of the results**

of clinical trials or non- clinical studies or our clinical trial designs and plans; • we may fail to establish an appropriate safety profile for a product candidate based on clinical or ~~preclinical~~ **nonclinical** data for such product candidates as well as data emerging from other therapies in the same class as our product candidates; and • the FDA or other regulatory authorities may require us to submit additional data such as long- term toxicology studies, **additional clinical data or additional manufacturing data** or impose other requirements before permitting us to initiate ~~a~~ clinical ~~trial~~ **trials or approving marketing / commercial sales** . Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND ~~,~~ ~~BLA~~ or similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional ~~preclinical~~ **nonclinical** studies **or clinical trials** or we are required to satisfy other FDA requests prior to commencing **future planned** clinical trials, the start of ~~our first~~ **such planned** clinical trials may be delayed **or such planned clinical trials may be commenced in a modified manner** . Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any **future** clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional ~~preclinical~~ **nonclinical** studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. **Even if we conduct such additional nonclinical studies or clinical trials, the FDA or other regulatory authorities could determine that the data from our nonclinical studies or clinical trials are insufficient to support the safety and efficacy of our product candidates.** There are equivalent processes and risks applicable to clinical trial applications in other countries **outside of** ~~, including countries in~~ the ~~EU~~ **United States., which may require us to complete additional nonclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect** . We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our product candidates. We or our current or future collaborators' inability to complete development of, or commercialize our product candidates, or significant delays in doing so, could have a material and adverse effect on our business, financial condition, results of operations and prospects. We are substantially dependent on the success of our ~~two~~ **three** most advanced programs, SPY001 ~~and~~ **,** SPY002 ~~,~~ and **SPY003, alone** ~~our~~ **or** ~~anticipated~~ **in combination, and our current and planned** clinical trials of such programs may not be successful. Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our ~~two~~ **three** most advanced programs, SPY001 ~~and~~ **,** SPY002 **and SPY003, alone or in combination** . We exercised our Option with respect to the SPY001 ~~and~~ **,** SPY002 **and SPY003** programs on July 12, 2023 ~~and~~ **,** December 14, 2023, **and June 5, 2024,** respectively **. Additionally, in May 2024, we signed license agreements with Paragon for rights to royalty- bearing, world- wide, exclusive licenses to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting α4β7 integrin (SPY001 program) and TL1A (SPY002 program) and, in October 2024, we signed a license agreement for rights to a royalty- bearing, world- wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting IL- 23 (SPY003 program) in the field of IBD. The SPY003 License Agreement was subsequently amended and restated in February 2025 to, among other things, clarify each party' s rights and obligations with respect to license exclusivity and patent prosecution and correct certain clerical errors** . We are investing a majority of our efforts and financial resources into the research and development of these programs. We **initiated** ~~anticipate initiating~~ a Phase 1 clinical trial in healthy volunteers of SPY001 ~~in~~ **and announced** the **dosing of our** first ~~half of~~ **participant in June** 2024 ~~and~~ **. We also initiated a Phase 1 clinical trial in healthy volunteers** of SPY002 in the ~~second half~~ **fourth quarter** of 2024 **. We anticipate initiating a Phase 1 clinical trial in healthy volunteers of SPY003 in the first quarter of 2025, subject to regulatory feedback and approval. We also plan to initiate a Phase 2 platform trial of our product candidates in IBD beginning with monotherapies in mid- 2025 and subsequent planned addition of combination arms as well as a Phase 2 clinical trial of SPY002 in RA in mid- 2025** , each subject to ~~the filing of an IND or foreign equivalent and~~ regulatory **feedback and** approval. The success of our programs is dependent on observing ~~a~~ longer half- ~~life~~ **lives** of our product candidates in humans **and comparable or better safety and efficacy profiles** than other mAbs currently marketed ~~and~~ **or** in development ~~as we~~ **. We** believe ~~this~~ **these** longer half- ~~life has~~ **lives have** the potential to result in ~~a~~ more favorable dosing ~~schedule~~ **schedules** for our product candidates, assuming they successfully complete clinical development and obtain marketing approval. This is based in part on the assumption that the longer half- **lives** ~~life we have~~ observed in ~~non- human primates (" NHPs ")~~ will translate into ~~an~~ extended half- ~~life~~ **lives** of our product candidates in humans. To the extent we do not observe ~~this~~ **these** extended half- ~~life~~ **lives with favorable safety and efficacy profiles** when we dose humans with our product candidates, it would significantly and adversely affect the clinical and commercial potential of our product candidates. Our programs will require additional clinical development, evaluation of clinical, ~~preclinical~~ **nonclinical** and manufacturing activities, product development, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote these programs, or any other programs, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals. The success of our product candidates will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any current or future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of these product candidates, even if approved. If we are not successful in commercializing ~~our~~ SPY001 ~~or~~ **,** SPY002 ~~programs~~ **or SPY003, alone or in combination** , or are significantly delayed in doing so, our business will be materially harmed. If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our product candidates may be delayed and our expenses may increase and, as a result, our stock price may decline. From time to time, we estimate the

timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of ~~scientific~~ **nonclinical** studies and clinical trials, such as the expected timing for the anticipated ~~commencement~~ **completion** of our Phase 1 ~~study,~~ clinical trials in **healthy volunteers and topline data from our planned Phase 2 clinical trials in** IBD **and RA** , as well as the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control **, including positions that may be taken by or requirements of regulatory authorities** . If we do not meet these milestones as publicly announced, or at all, the commercialization of our product candidates may be delayed or never achieved and, as a result, our stock price may decline. Additionally, delays relative to our projected timelines are likely to cause overall expenses to increase, which may require us to raise additional capital sooner than expected and prior to achieving targeted development milestones. Any drug delivery device that we potentially use to deliver our product candidates may have its own regulatory, development, supply and other risks. We expect to deliver our product candidates via a drug delivery device, such as an injector or other delivery system. There may be unforeseen technical complications related to the development activities required to bring such a product to market, including primary container compatibility and / or dose volume requirements **. If our product candidates are intended to be used with drug delivery devices, we expect to utilize drug delivery devices authorized for marketing under clearances of approvals held by third parties** . Our product candidates may not be approved or may be substantially delayed in receiving approval if the devices that we choose to develop do not gain and / or maintain their own regulatory approvals or clearances. Where approval of the drug product and device is sought under a single application, the increased complexity of the review process may delay approval. In addition, some drug delivery devices are provided by single- source unaffiliated third- party companies. We may be dependent on the sustained cooperation and effort of those third- party companies both to supply the devices and, in some cases, to conduct the studies required for approval or other regulatory clearance of the devices. Even if approval is obtained **for our products** , we may also be dependent on those third- party companies continuing to maintain such approvals or clearances **, if required, for their drug delivery devices** once they have been received. Failure of third- party companies to supply the devices, to successfully complete studies on the devices in a timely manner, or to obtain or maintain required approvals or clearances of the devices could result in increased development costs, delays in or failure to obtain regulatory approval and delays in product candidates reaching the market or in gaining approval or clearance for expanded labels for new indications. Our approach to the discovery and development of our programs is unproven, and we may not be successful in our efforts to build a pipeline of programs with commercial value. Our approach to the discovery and development of the research programs with respect to which we have **signed a license agreement,** exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement **,** leverages clinically validated mechanisms of action and incorporates advanced antibody engineering to optimize half- life and other properties designed to overcome limitations of existing therapies. Our programs are purposefully designed to improve upon existing product candidates and products while maintaining the same ~~,~~ well- established mechanisms of action. However, the scientific research that forms the basis of our efforts to develop programs using half- life extension technologies, including YTE and LS amino acid substitutions, is ongoing and may not result in viable programs. We have limited clinical data on product candidates utilizing YTE and LS half- life extension technologies, especially in I & I indications, demonstrating whether they are safe or effective for long- term treatment in humans. The long- term safety and efficacy of these technologies and the extended half- ~~life~~ **lives** and exposure ~~profile~~ **profiles** of our programs compared to currently approved products ~~is~~ **are** unknown. We may ultimately discover that ~~utilizing~~ **our investigational products developed with** half- life extension technologies ~~for our specific targets and indications and any programs resulting therefrom~~ do not possess certain properties required for therapeutic effectiveness **and could lead to adverse effects** . ~~We~~ **Other than for our SPY001 program, we** currently have only ~~preclinical~~ **nonclinical** data regarding the increased half- life properties of our programs and ~~the same results~~ **a similar half- life extension** may not be seen in humans. In addition, programs using half- life extension technologies may demonstrate different chemical and pharmacological properties in participants than they do in laboratory studies. This technology and any programs resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. In addition, we may in the future seek to discover and develop programs that are based on novel targets and technologies that are unproven. If our discovery activities fail to identify novel targets or technologies for drug discovery, or such targets prove to be unsuitable for treating human disease, we may not be able to develop viable additional programs. We and our existing or future collaborators may never receive approval to market and commercialize any product candidate. Even if we or an existing or future collaborator obtains regulatory approval, the approval may be for targets, disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. If the products resulting from the research programs with respect to which we have **signed license agreements with Paragon,** exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement prove to be ineffective, unsafe or commercially unviable, ~~such~~ **our** programs **and pipeline** would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects. ~~Preclinical~~ **Nonclinical** and clinical development ~~involves~~ **involve** ~~a~~ lengthy and expensive ~~process~~ **processes** that ~~is~~ **are** subject to delays and ~~with~~ **may result in** uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our ~~preclinical~~ **nonclinical** studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete ~~preclinical~~ **nonclinical** studies and then conduct extensive clinical trials to demonstrate the

safety and efficacy of our product candidate in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the ~~preclinical~~ **nonclinical** study or clinical trial process. For example, we depend on the availability of NHPs to conduct certain ~~preclinical~~ **nonclinical** studies that we are required to complete prior to submitting an IND **or foreign equivalent** and initiating clinical development. There is ~~currently a global shortage of~~ **no guarantee that we will always be able to source** NHPs ~~available~~ for **our** drug development **activities on our preferred timelines** . **The** ~~This could cause the~~ cost of obtaining NHPs for our future ~~preclinical studies to~~ **nonclinical development activities could** increase significantly ~~and,~~ if ~~the~~ **short or long term** ~~shortage~~ **shortages** ~~continues~~ **occur in their availability. If we are unable to source NHPs on our preferred timelines** , **it** could ~~also~~ result in delays to our development timelines. **Similarly, we may experience difficulty in conducting our clinical trials as planned if we are unable to enroll a sufficient number of participants in any such trial as a result of variables outside of our control. See the risk factor titled " If we encounter difficulties enrolling participants in our current and future clinical trials, our clinical development activities could be delayed or otherwise adversely affected. "** Furthermore, a failure of one or more clinical trials can occur at any stage of testing. The outcome of ~~preclinical~~ **nonclinical** studies and early- stage clinical trials may not be predictive of the success of later clinical trials. Moreover, ~~preclinical~~ **nonclinical** and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in ~~preclinical~~ **nonclinical** studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. In addition, we expect to rely on participants to provide feedback on measures such as measures of **disease activity and measures of** quality of life, which are subjective and inherently difficult to evaluate. These measures can be influenced by factors outside of our control ~~,~~ and can vary widely from day to day for a particular participant, and from participant to participant and from site to site within a clinical trial. We cannot be sure that the FDA **, or comparable foreign regulatory authority, as applicable,** will agree with our clinical development ~~plan~~ **plans** . We plan to use the data from our **ongoing and** planned Phase 1 trials of our SPY001 ~~and~~ **,** SPY002 **and SPY003** programs in healthy volunteers to support Phase 2 trials in IBD **, RA** and other I & I indications. If the FDA **and / or comparable foreign regulatory authority** requires us to **materially modify our proposed trial designs,** conduct additional trials or enroll additional participants, our development timelines may be delayed. We cannot be sure that submission of an IND, ~~BLA~~ **CTA** or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate **them** ~~such clinical trials~~ . Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient ~~preclinical~~ **nonclinical** , toxicology or other in vivo or in vitro data ~~to support the initiation or continuation of clinical trials~~ ; delays in reaching a consensus with regulatory authorities on ~~study~~ **trial** design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with **current and** prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; **CRO personnel changes which could lead to operational delays or complications;** delays in identifying, recruiting and training suitable clinical investigators **and their study teams** ; delays in obtaining required **EC /** IRB approval at each clinical trial site; delays in manufacturing, testing, releasing, validating or importing / exporting sufficient stable quantities of our product candidates **or other supplies** for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA' s or any other regulatory authority' s good clinical practice requirements (" GCPs ") or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to facilities operated by a contract manufacturing organization (~~"~~ **"** CMO ~~"~~ **"**) and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and third parties being unwilling or unable to satisfy their contractual obligations to us. We could also encounter delays if a **planned** clinical trial is **required to be materially modified or** suspended or terminated by us, by the **ECs /** IRBs of the institutions in which such clinical trials are being conducted, by the **external** Data ~~Safety~~ Monitoring ~~Board~~ **Committee** , if any, for such clinical trial or by the FDA or comparable foreign regulatory authorities. Such authorities may suspend **, put on clinical hold** or terminate a clinical trial due to a number of factors, including **not aligning with or supporting our clinical trial designs or our** failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the programs, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates, if the results of these trials are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs. **A key element of our strategy is the development of intra- portfolio investigational drug combinations. If we are not successful in discovering, developing and commercializing investigational products that take advantage of different mechanisms of action to achieve superior outcomes relative to the use of monotherapies or other combination therapies, our ability to achieve our strategic objectives would likely be impaired. A key element of our strategy is to build a broad portfolio of investigational products that will allow for the development of intra- portfolio combinations.** We **believe that by developing or licensing these investigational products, we can control the combinations we pursue and, if and when approved, maximize the commercial potential of these combinations. However, these combinations have not been tested before and may fail to achieve superior outcomes relative to the use of single agents or other**

combination therapies, may exacerbate adverse events associated with one of the investigational products when used as monotherapy, may yield new adverse events not observed with either of the monotherapies, or may fail to demonstrate sufficient safety or efficacy in clinical trials to enable us to complete those clinical trials or obtain marketing approval for the combination therapy. In addition, demonstrating that our combinations are ~~researching~~ **superior to our single agents is likely necessary for marketing authorization of the combinations. However, comparing active treatments may be difficult to do in a controlled manner in our clinical trials, and we may be unable to interpret the results of comparisons between our combinations and single agents in a manner that satisfies regulatory requirements. Even if we are successful in developing combination therapies, competition from** ~~the~~ **other investigational products in the same class which are either already approved or further along in development than ours may prevent us from realizing the commercial** potential **of our combination therapies and prevent** ~~use~~ **us from achieving our strategic objectives. Development** of ~~complementary diagnostics~~ **combination therapies may present more or different challenges than development of monotherapies. We plan to pursue development of our investigational products** in ~~connection~~ **combination** with ~~the~~ **one or more additional products or investigational products. The** development of ~~our~~ **combination therapies may be more complex than the development of monotherapies and generally requires that sponsors demonstrate the contribution of each investigational** product ~~candidates,~~ **to the claimed effect** and ~~although~~ **the safety and efficacy of the combination as a whole. Regulatory authority requirements for the development of combination therapies may make the design and conduct of clinical trials more complex and / or burdensome, requiring more clinical trial participants and additional time and cost to complete than** we ~~do~~ **plan or anticipate. We also may** not **be able to meet the FDA' s** ~~currently~~ **current or future approval standards** ~~anticipate such diagnostics would be~~ required for **combination therapies** ~~the regulatory approval of any of our~~ **or combination products, if we decided to administer or package a combination therapy as a single drug** product ~~candidates~~ **. For example , under** ~~they~~ **the" combination rule", the FDA** may ~~be helpful~~ **not file or approve a fixed- dose combination product unless each component of a proposed drug product is shown** to ~~maximize~~ **make a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is safe and effective for the intended population. To satisfy** ~~the~~ **these requirements, the FDA typically requires a** clinical ~~and commercial success of our~~ **factorial trial, designed to assess the effects attributable to each drug in the combination** product ~~candidates and if we fail to develop such complementary diagnostics~~ **. This is particularly true when the ingredients are directed at the same sign** or ~~obtain regulatory approvals~~ **symptom of the disease or condition. The FDA has accepted a variety of approaches to satisfy the combination rule but the FDA has stated** that **factorial studies may be unethical (e. g., omitting a drug known to improve survival) or impractical (there may be too** ~~may~~ **many** ~~be required if~~ **components to conduct a factorial trial, meaning** ~~they~~ **the** ~~will~~ **trial cannot** be **conducted). The FDA has also stated that it may be possible to** ~~used~~ **use other types** ~~commercially alongside any~~ of ~~our product candidates~~ **clinical and nonclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination. In addition** , ~~our~~ **combination** products may **require dose selection** ~~not be as competitive or~~ **for** ~~commercially successful as~~ **each agent in** ~~they~~ **the combination** ~~could be. A complementary diagnostic is a medical device, often an in vitro device~~ , which ~~provides information that is valuable for the safe and effective use of a corresponding therapeutic drug or biologic product. A complementary diagnostic can be used to identify patients or subsets of patients who are most likely to benefit from the therapeutic product. A complementary diagnostic is generally developed in conjunction with the clinical program for an associated therapeutic product. The development path of a complementary diagnostic may include additional meetings with regulatory authorities, such as a pre- submission meeting and the requirement to submit an investigational device exemption application. In the case of a complementary diagnostic that is designated as " significant risk device, " approval of an investigational device exemption by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding product candidate. To be successful in developing, validating, obtaining approval of and commercializing a complementary diagnostic, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for complementary diagnostic tests on our own, we~~ may require **more** ~~additional personnel. We may rely on third parties for the design, development, testing, validation~~ and ~~manufacture of complementary diagnostic tests for our therapeutic product candidates that may benefit from such tests, the application for and receipt of any required regulatory approvals, and the commercial supply of these complementary diagnostics. Although we currently plan to focus our complementary diagnostic development program on diagnostics that may help to identity high~~ / ~~better responding patients for~~ **or larger groups of participants than single agents. Our** ~~our product candidates, we do not believe such complementary diagnostics will be required by regulatory authorities in connection with granting regulatory approval for our product candidates but may aid in~~ clinical trial ~~recruitment, post-~~ **and research efforts may not satisfy regulators' expectations of adequate exploration of dose ranging required for drug** approval **. Moreover,** ~~treatment decisions and maximizing~~ the ~~commercial success~~ **applicable requirements for approval** of **a combination therapy may differ from country to country. In the event that one of** our **investigational** ~~product~~ **products** ~~candidates. If we~~ **were to fail to demonstrate sufficient safety and efficacy data** or ~~third parties~~ **establish its contribution to the claimed effects of a combination therapy or if** we ~~engage~~ are unable to ~~successfully develop complementary diagnostics~~ **meet the FDA' s current or future approval standards required** for **combination therapies** ~~our~~ **or combination** ~~product~~ **products** ~~candidates, or experience delays~~ in ~~doing so: • a~~ **timely manner,** we **would need** ~~may be unable to maximize our potential~~ to identify ~~appropriate patients~~ **and research alternative monotherapy** ~~for~~ **or** ~~enrollment in~~ **combination treatments, run additional trials to produce supportive data** ~~our~~ **or modify existing** clinical ~~trials~~ **trial plans. In** ~~, which may adversely affect the development of our therapeutic product candidates; • if the FDA or other regulators determine that the safe and effective use of our therapeutic product candidates, if any, depends on the complementary diagnostics we develop then~~ **the** ~~we would have to~~

~~expend time and resources to obtain regulatory approval of such complementary diagnostics which could cause delays in the commercial launch or success of our product candidates; and • we may not realize the full commercial potential of any therapeutics that receive marketing approval. As a result of any of these events~~ **event** ~~, our business, financial condition, results of operations and prospects could be materially and adversely affected. To be successful in developing and commercializing therapeutic product candidates in combination with diagnostic candidates, we will need to address a number of scientific, technical, regulatory and logistical challenges. We currently anticipate that we or a collaborator may need to obtain marketing authorization from the FDA in order to legally market such diagnostics in the United States. As a company, we have little experience in the development of diagnostic tests and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates that receive marketing approval, and have never applied for or obtained regulatory clearance or approval of any such diagnostic tests. Given our limited experience in developing diagnostic tests, we may rely in part or in whole on third parties for their design, development and manufacture of such tests. Before a new medical device, or a new intended use of, claim for, or significant modification to an existing device, can be marketed in the United States, a company must first submit an application for and receive 510 (k) clearance pursuant to a premarket notification submitted under Section 510 (k) of the Federal Food, Drug, and Cosmetic Act (" FDCA "), de- novo classification, or PMA approval from FDA, unless an exemption applies. The PMA approval pathway, which we expect to pursue for our complementary diagnostic product candidates, requires an applicant to demonstrate the safety and effectiveness of the product based, in part, on valid scientific evidence, including, but not limited to, technical, preclinical, and clinical data. The 510 (k) pathway requires a FDA finding that the test is substantially equivalent to a legally marketed predicate device. If no legally marketed predicate can be identified to enable use of the 510 (k) pathway, the device is automatically classified under the FDCA into Class III, which generally requires PMA approval. However, for low- to moderate- risk novel devices, FDA allows for the possibility of marketing authorization through the " de novo classification " process rather than requiring the device to be subject to PMA approval. Products that are approved through a PMA application generally need prior FDA approval before modifications can be made that affect safety or effectiveness, and certain modifications to a 510 (k)- cleared device may also require FDA premarket review before the modified product can be marketed. If~~ we are unable to **do so** ~~successfully develop, obtain regulatory clearance for~~ **or** ~~and~~ **are unable to do so on** ~~commercialize~~ **commercially reasonable terms** ~~diagnostics to pair with our~~ **or we are unable** ~~therapeutic product candidates, it could adversely impact our ability~~ to **continue** ~~develop and generate revenue from our product candidates. We may pursue~~ development of ~~combination~~ **one or more of investigational** products **,** ~~that require coordination within the FDA and comparable foreign regulatory authorities for review of its device and biologic components. Although the FDA and comparable foreign regulatory authorities have systems in place for the review and approval of combination products such as ours~~ **our business** ~~, we may experience delays in the development~~ and **prospects** ~~commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process. Of note, prior clearance or approval of one component of a combination product does not increase the likelihood that FDA will approve a later product combining the previously cleared product or approved active ingredient with a novel active ingredient. If we encounter difficulties enrolling participants in our future clinical trials, our clinical development activities could~~ **would** be **materially harmed** ~~delayed or otherwise adversely affected~~. We may experience difficulties in ~~patient~~ participant enrollment in our **current and** future clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of participants who remain in the trial until its conclusion. The enrollment of participants ~~in future trials for any of our programs~~ will depend on many factors, including if participants choose to enroll in clinical trials, rather than using approved products, or if our competitors have ongoing clinical trials for programs that are under development for the same indications as our programs, and participants instead enroll in such clinical trials. Additionally, the number of participants required for clinical trials of our programs may be larger than we anticipate ~~, especially if regulatory bodies require the completion of non- inferiority or superiority trials~~. Even if we are able to enroll a sufficient number of participants for our **current or** future clinical trials, we may have difficulty maintaining participants in our clinical trials. Our inability to enroll or maintain a sufficient number of participants would result in significant delays in completing clinical trials or receipt of marketing approvals ~~and~~ **,** increased development costs or **our cessation of** ~~may require us to abandon~~ one or more clinical trials altogether. Preliminary, " topline " or interim data from our clinical trials that we announce or publish from time to time may change as more participant data become available and are subject to audit and verification procedures. From time to time, we may publicly disclose preliminary or topline data from our ~~preclinical~~ **nonclinical** studies and clinical trials, which are based on a preliminary analysis of then- available data **. The** ~~, and the~~ results and related findings and conclusions are subject to change following a more comprehensive review ~~of the~~ **or taking into account additional** data **that becomes available** . ~~We~~ **In reviewing preliminary or topline data, we** also make assumptions, estimations, calculations and conclusions as part of our analyses **that may change once a** ~~of these data without the opportunity to fully and carefully evaluate~~ complete data **set is available** . As a result, the preliminary or topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated or subsequently made subject to audit and verification procedures. Any preliminary or topline data should be viewed with caution until the final data are available. ~~From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data are subject to the risk that one or more of the clinical outcomes may materially change as participant enrollment continues and more participant data become available or as participants from our clinical trials continue other treatments.~~ Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular product candidate, the approvability or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular ~~preclinical~~ **nonclinical** study or clinical trial is based on what is typically extensive information, and you or others may not

agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary, topline or interim data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. Our **current and** future clinical trials or those of our future collaborators may reveal significant adverse events or undesirable side effects not seen in our ~~preclinical~~ **nonclinical** studies and may result in a safety profile that could halt clinical development, inhibit regulatory approval or limit commercial potential or market acceptance of any of our product candidates. Results of our **non- clinical studies or** clinical trials could reveal a high and unacceptable severity and prevalence of side effects, adverse events or unexpected characteristics ~~. While~~ **at any point in time during the development process for** our ~~preclinical~~ **product candidates. We cannot assure you that the future results of our nonclinical** studies ~~in NHPs have~~ **or clinical trials will** not **reveal** ~~shown any~~ such characteristics ~~to date, we have not yet initiated any clinical trials in humans~~. If significant adverse events or ~~other~~ **undesirable** side effects are observed in any of our **current or** future **non- clinical studies or** clinical trials, we may have difficulty recruiting participants to such trials, participants may drop out of our trials, or we may be required to **cease** ~~abandon the trials~~ or **materially modify** our development efforts of one or more programs ~~altogether~~. We, the FDA or other applicable regulatory authorities, or an **EC /** IRB, may suspend **or require the material modification of** any clinical trials of any program at any time for various reasons, including a belief that **participants** ~~subjects or patients~~ in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential products developed in the biotechnology industry that initially showed therapeutic promise in early-stage studies and trials have later been found to cause side effects that prevented their further development. Other potential products have shown side effects in ~~preclinical~~ **nonclinical** studies, which side effects do not present themselves in clinical trials in humans. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. In addition, an extended half- life could prolong the duration of undesirable side effects, which could also inhibit market acceptance. Treatment- emergent adverse events could also affect participant recruitment or the ability of enrolled ~~subjects~~ **participants** to complete our clinical trials or could result in potential product liability claims. Potential side effects associated with our product candidates may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from our product candidates may not be normally encountered in the general patient population and by medical personnel. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly **. Our product candidates have mechanisms of action that have been associated with certain adverse reactions in patients. For example, nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities are the most common adverse reactions noted with Entyvio, which is in the same drug class as SPY001 and is approved for the treatment of moderately to severely active ulcerative colitis in adults and of moderately to severely active Crohn' s disease in adults. In addition, mAbs targeting TL1A such as our product candidate SPY002, in clinical research are associated with patient adverse reactions that most commonly include headache, nasopharyngitis, arthralgia, and back pain. Finally, for Skyrizi, which is in the same drug class as SPY003 and is approved for the treatment of moderately to severely active ulcerative colitis in adults and of moderately to severely active Crohn' s disease in adults, the most common adverse reactions are upper respiratory infections, headache, arthalgia, injection site reactions, abdominal pain, anemia, pyrexia, back pain, arthropathy, and urinary tract infection in patients with Crohn' s disease and arthralgia, pyrexia, injection site reactions, and rash in patients with UC. Patients in our clinical trials for SPY001, SPY002 and SPY003, or combinations thereof, may experience similar or additional adverse reactions** . In addition, even if we successfully advance our product candidates or any future product candidates through clinical trials, such trials will only include a limited number of participants and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of participants are exposed to the product ~~candidate~~ after approval. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of using **any of** our ~~product~~ **products** ~~candidates~~ over a multi- year period. If any of the foregoing events occur or if one or more of the research programs with respect to which we have **signed a licensed agreement for or** exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects. We may expend our limited resources to pursue a particular program and fail to capitalize on programs that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus our research and development efforts on certain selected programs. For example, we are initially focused on our most advanced programs, SPY001 ~~and ,~~ SPY002 **and SPY003, including combinations thereof** . As a result, we may forgo or delay pursuit of opportunities with other programs that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any approved products resulting from our current programs or any future program may not achieve adequate market acceptance among clinicians, patients, healthcare third- party payors and others in the medical community necessary for commercial success and we may not generate any future revenue from the sale or licensing of such products. Even if regulatory approval is obtained for a product candidate resulting from one of our current or future programs, they may not gain market acceptance

among physicians, patients, healthcare payors or the medical community. We may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether it will otherwise be accepted in the market. There are several approved products and product candidates in later stages of development for the treatment of IBD **and the treatment of RA** . However, our programs incorporate advanced antibody engineering to optimize the half- life and formulation of antibodies; to date, no such antibody has been approved by the FDA for the treatment of IBD **or RA** . Market participants with significant influence over acceptance of new treatments, such as clinicians and third- party payors, may not adopt a biologic that incorporates half- life extension for our targeted indications, and we may not be able to convince the medical community and third- party payors to accept and use, or to provide favorable reimbursement for, any programs developed by us or our existing or future collaborators. An extended half- life may make it more difficult for patients to change treatments and there is a perception that half- life extension could exacerbate side effects, each of which may adversely affect our ability to gain market acceptance. Market acceptance of our product candidates will depend on many factors, including factors that are not within our control. Sales of medical products also depend on the willingness of clinicians to prescribe the treatment. We cannot predict whether clinicians, clinicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective, cost effective or less burdensome as compared with competing treatments. If any current or future product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable. ~~Certain~~ **Some** of our programs may compete with our other programs, which could negatively impact our business and reduce our future revenue. We ~~are developing~~ **have multiple** product candidates **in development** for the same indication ~~:~~ **,** IBD, and **are planning to develop one product candidate (SPY002) for RA. We** may in the future develop our programs for other I & I indications. Each such program targets a different mechanism of action. However, developing multiple programs for a single indication may negatively impact our business if the programs compete with each other. For example, if multiple programs are conducting clinical trials at the same time, they could compete for the enrollment of participants. In addition, if multiple product candidates are approved for the same indication, they may compete for market share, which could limit our future revenue. We ~~plan to~~ **are conducting and may** conduct **future** clinical trials for **our** programs at sites outside the United States, and the FDA may not accept data from trials conducted in such locations. We **are conducting our Phase 1 clinical trials for SPY001 and SPY002 in Canada and the United States, and we** may choose to conduct one or more of our future clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well ~~-~~ designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U. S. population, and the data must be applicable to the U. S. population and U. S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U. S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time- consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated. Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled participants in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs that could restrict or limit our ability to conduct our clinical trials, the administrative burdens of conducting clinical trials under multiple sets of foreign regulations, foreign exchange fluctuations ~~;~~ ~~diminished protection of intellectual property in some countries~~ , as well as political and economic risks relevant to foreign countries. The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired. The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our most advanced product candidates, SPY001 ~~and~~ **,** SPY002 **and SPY003** , we must demonstrate through lengthy, complex and expensive ~~preclinical~~ **nonclinical** studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional ~~preclinical~~ **nonclinical** , clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for

approval; serious and unexpected drug- related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; we may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from ~~preclinical~~ **nonclinical** studies or clinical trials; the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and / or the specifications of our product candidates; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, including failing to approve the most commercially promising indications, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates and our ability to generate revenue will be materially impaired. We may not be able to meet requirements for the chemistry, manufacturing and control of our programs. In order to receive approval of our products by the FDA and comparable foreign regulatory authorities, we must show that we and our contract manufacturing partners are able to characterize, control and manufacture our drug products **and drug delivery devices** safely and in accordance with regulatory requirements. This includes manufacturing the active ingredient, developing an acceptable formulation **and drug delivery device** , manufacturing the drug product **and drug delivery device** , performing tests to adequately characterize the formulated product, documenting a repeatable manufacturing process, **meeting facility, process, testing validation and commercialization requirements,** and demonstrating that our drug products meet **standards for parenteral administration as well as** stability **and quality** requirements. Meeting these chemistry, manufacturing and control requirements is a complex task that requires specialized expertise. If we are not able to meet the chemistry, manufacturing and control requirements, we may not be successful in getting our products approved. Our product candidates for which we intend to seek approval as biologics may face competition sooner than anticipated. The Patient Protection and Affordable **Care** Act, as amended by the Healthcare and Education Reconciliation Act (the " ACA "), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (" BPCIA "), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA- licensed reference biological product. Under the BPCIA, an application for a highly similar or " biosimilar " product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12- year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor' s own ~~preclinical~~ **nonclinical** data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of their product. We believe that any of our product candidates approved as biologics under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not ~~consider~~ **accord** our product candidates ~~to be~~ reference ~~products~~ **product** ~~for competing~~ **exclusivity relative to biosimilar** products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any reference products in a way that is similar to traditional generic substitution for non- biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. Even if we receive regulatory approval of our product candidates, we will be subject to extensive ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post- approval ~~study~~ **trial** or risk management requirements. For example, the FDA may require a risk evaluation and mitigation strategy ~~(" REMS")~~ in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or comparable foreign regulatory authorities approve our product candidates, our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export will be subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as on- going compliance with current cGMPs **, good pharmacovigilance practices (" GVPs ")** and GCPs for any ~~clinical~~ **post- approval** trials that we conduct following approval.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs. **Following approval, sponsors are also subject to continual review and periodic, unannounced inspections for compliance with GVPs.** If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing ~~.~~ **,** restrictions on our ability to conduct ~~clinical~~ **post- approval** trials, including full or partial ~~clinical~~ holds on ongoing or planned trials, restrictions on the manufacturing process, warning or untitled letters, civil and criminal penalties, injunctions, product seizures, detentions or import bans, voluntary or mandatory publicity requirements and imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. **We may face difficulties from healthcare legislative reform measures and other changes in law.** Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay **development of or** regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, ~~we~~ **our product candidates may be delayed in obtaining regulatory approval or** may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability **. In addition, the impact of legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the current government administration on us and the pharmaceutical industry as a whole is unclear. These government actions could cause delays in our business plans, increase cost of execution of our business plans or otherwise have a material adverse affect on our business. For example, if legislation similar to the BIOSECURE Act is passed with terms that require us to switch or move development of our product candidates from one CMO to another, we may incur additional development costs or delays in manufacturing product for clinical trials or commercialization** . See the section titled " Business – Government Regulation – Healthcare Reform " **in this Annual Report on Form 10- K** for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. See the section titled " Business – Government Regulation – Other Healthcare Laws and Compliance Requirements " **in this Annual Report on Form 10- K** for a more detailed description of the laws that may affect our ability to operate. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, integrity oversight and reporting obligations to resolve allegations of non- compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Even if we are able to commercialize any product candidates, due to unfavorable pricing regulations and / or third- party coverage and reimbursement policies, we may not be able to offer such product candidates at competitive prices **,** which would seriously harm our business. We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any product candidates that we may develop will depend in part on the extent to which reimbursement for these product candidates and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and other third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. These entities may create preferential access policies for a competitor' s product, including a branded or generic / biosimilar product, over our products in an attempt to reduce their costs, which may reduce our commercial opportunity. Additionally, if any of our product candidates are approved and we are found to have improperly promoted off- label uses of those product candidates, we may become subject to significant liability, which would materially adversely affect our business and financial condition. See the sections titled " Business – Government Regulation – Coverage and Reimbursement " and " Business – ~~Other~~ Government Regulation ~~Outside of the United States~~ – Regulation in the European Union " **in this Annual Report on Form 10- K** for a more detailed description of the government regulations and third **-** party payor practices that may affect our ability to commercialize our product candidates. We are subject to U. S. and certain foreign export and import controls, sanctions, embargoes, anti- corruption laws, and anti- money laundering laws and regulations. We can face criminal liability and other serious consequences for violations, which can harm our business. We are subject to export control and import laws and regulations, including the U. S. Export Administration Regulations, U. S.

Customs regulations, various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls, the U. S. Foreign Corrupt Practices Act of 1977, as amended, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, the USA PATRIOT Act, **the U. S. Physician Payments Sunshine Act** and other state and national anti- bribery and anti- money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to or from recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any. In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that compare the cost- effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third- party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected. **If** ~~Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as~~ the UK ~~determines which~~ **or certain** EU **member states** ~~laws to replicate or replace. If the UK~~ were to significantly alter ~~its~~ **their** regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs. A breakthrough therapy, fast track, or other expedited designation for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that those product candidates will receive marketing approval. We may seek a breakthrough therapy, fast track, or other designation for appropriate product candidates. Designations such as these are within the discretion of the FDA, or other comparable regulatory authorities. The receipt of a designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify under one of FDA' s designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. See the section titled " Business – Government Regulation – **United States Biologics Regulation –** Expedited Development and Review Programs " **in this Annual Report on Form 10- K** for a more detailed description of the process for seeking expedited designations such as fast track or breakthrough therapy designations. Our ability to obtain and protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage. We rely upon a combination of patents, trademarks, trade secret protection, confidentiality agreements **, license agreements, including the License Agreements,** and the Paragon Agreement to protect the intellectual property related to our programs and technologies and to prevent third parties from competing unfairly with us. Our success depends in large part on our ability to obtain and maintain patent protection for our platform technologies, programs and their uses, as well as our ability to operate without infringing on or violating the proprietary rights of others. We own and have licensed rights to pending patent applications and expect to continue to file patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business. However, we may not be able to protect our intellectual property rights throughout the world and the legal systems in certain countries may not favor enforcement or protection of patents, trade secrets and other intellectual property. Filing, prosecuting and defending patents on programs worldwide would be expensive and our intellectual property rights in some foreign jurisdictions can be less extensive than those in the United States; the reverse may also occur. As such, we may not have patents in all countries or all major markets and may not be able to obtain patents in all jurisdictions even if we apply for them. Our competitors may operate in countries where we do not have patent protection and can freely use our technologies and discoveries in such countries to the extent such technologies and discoveries are publicly known or disclosed in countries where we do have patent protection or pending patent applications. Our pending and future patent applications may not result in patents being issued. Any issued patents may not afford sufficient protection of our programs or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or programs. Even if these patents are granted, they may be difficult to enforce. Further, any issued patents that we may license or own covering our programs could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the United States Patent and Trademark Office (" USPTO "). Further, if we encounter delays in our clinical trials or delays in obtaining regulatory approval, the period of time during which

we could market our product candidates under patent protection would be reduced. Thus, the patents that we may own and license may not afford us any meaningful competitive advantage. In addition to seeking patents for some of our technology and programs, we may also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third- party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or state actors and those affiliated with or controlled by state actors. In addition, while we undertake efforts to protect our trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time- consuming litigation could be necessary to enforce and determine the scope of our proprietary rights and failure to obtain or maintain trade secret protection could adversely affect our competitive business position **. Enforcing a claim that a party illegally obtained and is using our trade secrets is challenging and the outcome is unpredictable. In addition, courts outside of the U. S. may be less willing to protect trade secrets** . Lastly, if our trademarks and trade names are not registered or adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. We may not be successful in obtaining or maintaining necessary rights to our programs through acquisitions and in- licenses. Because our development programs currently do and may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in- license, or use these third- party proprietary rights. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary for our programs. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies may 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 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** ~~do obtain~~ , we may have to abandon development of the relevant program, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our programs, there may be times when the filing and prosecution activities for patents and patent applications relating to our programs are controlled by our current and future licensors or collaboration partners. If any of our current and future licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our current and future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution. Our current and future licensors may rely on third- party consultants or collaborators or on funds from third parties such that our current and future licensors are not the sole and exclusive owners of the patents we in- license. If other third parties have ownership rights to our current and future in- licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, programs, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our current technology, manufacturing methods, programs, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties, which could be significant. Disputes may arise between us and our current and future licensors regarding intellectual property subject to a license agreement, including: the scope of rights granted under the license agreement and other interpretation- related issues; whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; our right to sublicense patents and other rights to third parties; our right to transfer or assign the license; the inventorship and ownership of inventions and know- how resulting from the joint

creation or use of intellectual property by our current and future licensors and us and our partners; and the priority of invention of patented technology. We may be subject to patent infringement claims or may need to file claims to protect our intellectual property, which could result in substantial costs and liability and prevent us from commercializing our potential products. Because the intellectual property landscape in the biotechnology industry is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate and guarantee that we can operate without infringing on or violating third **-** party rights. If certain of our product candidates are ultimately granted regulatory approval, patent rights held by third parties, if found to be valid and enforceable, could be alleged to render one or more of our product candidates infringing. If a third party successfully brings a claim against us, we may be required to pay substantial damages, be forced to abandon any affected product candidate and / or seek a license from the patent holder. In addition, any intellectual property claims (e. g. patent infringement or trade secret theft) brought against us, whether or not successful, may cause us to incur significant legal expenses and divert the attention of our management and key personnel from other business concerns. We cannot be certain that patents owned or licensed by us will not be challenged by others in the course of litigation. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise funds and on the market price of our common stock. Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time- consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court or administrative body may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent' s claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court or administrative body may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. Further, we may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition, if our programs are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our future licensees and other parties with whom we have business relationships and we may be required to indemnify those parties for any damages they suffer as a result of these claims, which may require us to initiate or defend protracted and costly litigation on behalf of licensees and other parties regardless of the merits of such claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties or may be required to obtain licenses for the products they use. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. We may be subject to claims that we have wrongfully hired an employee from a competitor or that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties. As is common in the biotechnology industry, in addition to our employees, we engage the services of consultants to assist us in the development of our programs. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. ~~We~~ **Despite our training and compliance efforts, we** could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know- how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non- solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our programs, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act (the " Leahy- Smith Act ") could increase the uncertainties and costs surrounding the prosecution of our owned and in- licensed patent applications and the maintenance, enforcement or defense of our owned and in- licensed issued patents. The Leahy- Smith Act includes a number of significant changes to United States patent law. These changes

include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO- administered post-grant proceedings, including post- grant review, inter partes review and derivation proceedings. 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 Act, the United States transitioned to a first- to- file system in which, assuming that the other statutory 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. As such, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U. S. Supreme Court and U. S. Court of Appeals for the Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations, including in the antibody arts. For example, the United States Supreme Court in Amgen, Inc. v. Sanofi (Amgen) recently held that Amgen' s patent claims to a class of antibodies functionally defined by their ability to bind a particular antigen were invalid for lack of enablement where the patent specification provided twenty- six exemplary antibodies, but the claimed class of antibodies covered a " vast number " of additional antibodies not disclosed in the specification. The Court stated that if patent claims are directed to an entire class of compositions of matter, then the patent specification must enable a person skilled in the art to make and use the entire class of compositions. This decision makes it unlikely that we will be granted U. S. patents with composition of matter claims directed to antibodies functionally defined by their ability to bind a particular antigen. Even if we are granted claims directed to functionally defined antibodies, it is possible that a third party may challenge our patents, when issued, relying on the reasoning in Amgen or other recent precedential court decisions. Additionally, there have been proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U. S. Congress, the federal courts ~~and~~ **,** the USPTO **and the relevant law- making bodies in other countries** , the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future. Geopolitical instability in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of patent applications and the maintenance, enforcement or defense of issued patents. For example, the United States and foreign government actions related to Russia' s invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit- making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. In addition, a European Unified Patent Court (" UPC ") entered into force on June 1, 2023. The UPC is a common patent court that hears patent infringement and revocation proceedings effective for member states of the EU. This could enable third parties to seek revocation of a European patent in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. Although we do not currently own any European patents or applications **for our current pipeline** , if we obtain such patents and applications in the future, any such revocation and loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce or defend the validity of any European patents we may obtain. We may decide to opt out from the UPC any future European patent applications that we may file and any patents we may obtain. If certain formalities and requirements are not met, however, such European patents and patent applications could be challenged for non- compliance and brought under the jurisdiction of the UPC. We cannot be certain that future European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Obtaining and maintaining patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and / or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and / or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly

legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our programs, our competitive position would be adversely affected. We may not identify relevant third- party patents or may incorrectly interpret the relevance, scope or expiration of a third- party patent, which might adversely affect our ability to develop and market our products. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third- party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third- party patent or may incorrectly predict whether a third ~~-~~party' s pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our issued patents or our pending applications, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co- inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our programs or as a result of questions regarding co- ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and / or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Our current and future licensors may have relied on third- party consultants or collaborators or on funds from third parties, such as the U. S. government, such that our licensors are not the sole and exclusive owners of the patents we in- licensed ~~. For example, certain intellectual property we license from the University of Texas at Austin includes inventions that were made with U. S. government support~~ . The U. S. government therefore has certain rights in such inventions under the applicable funding agreements and under applicable law. If other third parties have ownership rights or other rights to our in- licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Patent terms may be inadequate to protect the competitive position of our product candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non- provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Our current or future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. We rely on collaborations and licensing arrangements with third parties, including our arrangement with Paragon. If we are unable to maintain these collaborations or licensing arrangements, or if these collaborations or licensing arrangements are not successful, our business could be negatively impacted. We currently rely on our collaborations and licensing arrangements with third parties, including Paragon, for a substantial portion of our discovery capabilities and in- licenses. Collaborations or licensing arrangements that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators or licensors. If any of our collaborators or licensors experiences delays in performance of, or fails to perform its obligations under their agreement with us, disagrees with our interpretation of the terms of such agreement or terminates their agreement with us, the research programs with respect to which we have **signed license agreements for or** exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement and development timeline could be adversely affected. If we fail to comply with any of the obligations under our collaborations or license agreements, including payment terms and diligence terms, our collaborators or licensors may have the right to terminate such agreements, in which event we may lose intellectual property rights and may not be able to develop,

manufacture, market or sell the products covered by our agreements or may face other penalties under our agreements. Our collaborators and licensors may also fail to properly maintain or defend the intellectual property we have licensed from them, if required by our agreement with them, or even infringe upon, our intellectual property rights, leading to the potential invalidation of our intellectual property or subjecting us to litigation or arbitration, any of which would be time- consuming and expensive and could harm our ability to commercialize our product candidates. In addition, collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our programs and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours. As part of our strategy, we plan to evaluate additional opportunities to enhance our capabilities and expand our development pipeline or provide development or commercialization capabilities that complement our own. We may not realize the benefits of such collaborations, alliances or licensing arrangements. Any of these relationships may require us to incur non- recurring and other charges, increase our near and long- term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. We may face significant competition in attracting appropriate collaborators, and more established companies may also be pursuing strategies to license or acquire third- party intellectual property rights that we consider attractive. These companies may have a competitive advantage over us due to their size, financial 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. Whether we reach a definitive agreement for a collaboration will depend upon, among other things, our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Collaborations are complex and time- consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical and biotechnology companies has reduced the number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market. We currently rely, and plan to rely in the future, on third parties to conduct and support our ~~preclinical~~ **nonclinical** studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates. We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract testing labs and strategic partners, to conduct and support our ~~preclinical~~ **nonclinical** studies and clinical trials under agreements with us. We will rely heavily on these third parties over the course of our ~~preclinical~~ **nonclinical** studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these ~~preclinical~~ **nonclinical** studies and clinical trials and the management of data developed through ~~preclinical~~ **nonclinical** studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third- party contractors and CROs are required to comply with **GLP,** GCP **and GVP** regulations, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our programs in clinical development. If we or any of these third parties fail to comply with applicable **GLP,** GCP **and GVP** regulations, the **nonclinical and** clinical data generated in our **nonclinical studies and** clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional **nonclinical and** clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our **nonclinical studies and** clinical trials comply with **GLP,** GCP **and GVP** regulations. In addition, our **nonclinical studies and** clinical trials must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat **nonclinical studies and** clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. Any third parties conducting our **nonclinical studies and** clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our programs. These third parties may be involved in mergers, acquisitions or similar transactions and may have relationships with other commercial entities, including our competitors, for whom they may also be conducting **nonclinical studies,** clinical trials or other product development activities, which could negatively affect their performance on our behalf and the timing thereof and could lead to products that compete directly or indirectly with our current or future product candidates. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our **nonclinical and** clinical protocols or regulatory requirements or for other reasons, our **nonclinical studies and** clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. In addition, we currently rely on foreign CROs and CMOs, including WuXi Biologics, and will likely continue to rely on foreign CROs and CMOs in the future. **We or the** ~~Foreign~~ **foreign CROs or** CMOs **we work with** may be subject to U. S. legislation, including the **potential passing of an act similar to the previously** proposed BIOSECURE ~~bill~~ **Act, sanctions** , trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies **or disrupt our supply chain. If we are not able to secure supply of our product candidates as a result of applicable legislation, this could result in a material adverse effect on our Company** . For example, the biopharmaceutical industry in China is strictly regulated by the Chinese government. Changes to Chinese regulations or

government policies affecting biopharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China which could have an adverse effect on our business, financial condition, results of operations and prospects. Evolving changes in China' s public health, economic, political, and social conditions and the uncertainty around China' s relationship with other governments, such as the United States and the UK, could also negatively impact our ability to manufacture our product candidates for our planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause us to delay our clinical development programs. We currently rely and expect to rely in the future on the use of manufacturing suites in third- party facilities or on third parties to manufacture our product candidates, and we may rely on third parties to produce and process our products, if approved. Our business could be adversely affected if we are unable to use third- party manufacturing suites or if the third- party manufacturers encounter difficulties in production. We do not currently own any facility that may be used as our clinical or commercial manufacturing and processing facility and must currently rely on CMOs to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our programs, if approved. We currently have a sole source relationship for our supply of the SPY001 **and SPY003 programs and one of the molecules in our SPY002** program. If there should be any disruption in such supply arrangement, including any adverse events affecting our ~~sole supplier~~ **suppliers**, it could have a negative effect on the clinical development of our programs and other operations while we work to identify and qualify ~~an~~ alternate supply ~~source~~ **sources**. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or comparable foreign regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and **other** 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 approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs ~~,~~ **and** delays, and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations. Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, **proposed or actual legislative changes or requirements,** or as a result of labor disputes or unstable political environments. If any CMOs on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. In addition, our CMOs **and other third parties** are responsible for transporting temperature- controlled materials that can be inadvertently degraded during transport due to several factors, rendering certain batches unsuitable for trial use for failure to meet, among others, our integrity and purity specifications. We and any of our CMOs may also face product seizure or detention or refusal to permit the import or export of products. Our business could be materially adversely affected by business disruptions to our third- party providers that could materially adversely affect our anticipated timelines, potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our ~~preclinical~~ **nonclinical** studies and clinical trials or the approval of any of our product candidates by the FDA, ~~result~~ **resulting** in higher costs or adversely impact commercialization of our product candidates. See the section titled " Business – Manufacturing **and Supply** " **in this Annual Report on Form 10- K** for a more detailed description of our manufacturing plans and assumptions and the factors that may affect the success of our programs. In order to successfully implement our plans and strategies, we will need to grow the size of our organization and we may experience difficulties in managing this growth. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of ~~preclinical~~ **nonclinical** and clinical drug development, technical operations, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial personnel and 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 working together 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. We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. We are a ~~preclinical~~ --- **clinical** stage biotechnology company with a limited operating history, and, as of December 31, ~~2023~~ **2024**, we had ~~30~~ **65** employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any ~~of our management team~~ **such officers and other principal** members may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. Attracting and retaining qualified personnel will also be critical to our success, including with respect to any strategic transaction that we may pursue. 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~~ **personnel** 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, facilitate regulatory approval of and commercialize 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 discovery and nonclinical and clinical development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties. Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable foreign regulatory authority, and may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we fail to comply with the regulatory requirements in international markets and receive applicable marketing approvals, 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 will be adversely affected. Moreover, even if we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to the risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries. Our estimates of market opportunity and forecasts of market growth may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all. Our market opportunity estimates and growth forecasts are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. Our estimates and forecasts relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet our size estimates and growth forecasts, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties. Our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. ~~We~~ **Despite our employee training and compliance programs, we** are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors acting for or on our behalf may engage in misconduct or other improper activities. We have adopted a code of conduct and ethics, **policies, standard operating procedures and other compliance efforts** but it is not always possible to identify and deter misconduct by these parties and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Our internal information technology systems, or those of any of our CROs, manufacturers, other contractors or consultants, third **-** party service providers, or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations. In the ordinary course of our business, we and the third parties upon which we rely collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) proprietary, confidential, and sensitive data, including personal data, intellectual property, trade secrets, and other sensitive data (collectively, sensitive information). Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and those of our third- party CROs, other contractors (including sites performing our clinical trials), third **-** party service providers and supply chain companies, and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and / or other third parties, or from cyber-attacks by malicious third parties, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, and the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, ability to provide our products or services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. To the extent that any disruption or security breach were to result in

loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. Further, our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored. Our fully- remote workforce may create additional risks for our information technology systems and data because our employees work remotely and utilize network connections, computers, and devices working at home, while in transit and in public locations. Additionally, business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. We rely on third- party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third- party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third- party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and / or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause stakeholders (including investors and potential customers) to stop supporting our platform, deter new customers from products, and negatively impact our ability to grow and operate our business. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims. Under ~~Section~~ **Sections** 382 **and 383** of the Internal Revenue Code of 1986, as amended (" the Code"), if a corporation undergoes an " ownership change, " generally defined as a greater than 50 % change (by value) in its equity ownership over a three- year period, the corporation' s ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre- change tax attributes (such as research tax credits) to offset its post- change income or taxes may be limited. Upon certain events since our conversion from a Delaware limited liability company to a Delaware corporation in 2015, it is possible that we may have triggered an " ownership change " limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which are outside of our control). As a result, if we earn net taxable income, our ability to use our pre- change NOLs and other pre- change tax attributes to offset U. S. federal taxable income or taxes may be subject to limitations, which could potentially result in increased future tax liability to us. ~~Our NOLs and other tax attributes arising before our conversion from a Delaware limited liability company to a Delaware corporation in 2015 also may be limited by the Separate Return Limitation Year rule, which could increase our U. S. federal tax liability.~~ In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. We are subject to stringent and changing laws, regulations and standards, and contractual obligations relating to privacy, data protection, and data security. The actual or perceived failure to comply with such obligations could lead to government enforcement actions (which could include civil or criminal penalties), fines and sanctions, private litigation and / or adverse publicity and could negatively affect our operating results and business. We, and third parties who we work with **,** are or may become subject to numerous domestic and foreign laws, regulations, and standards relating to privacy, data protection, and data security, the scope of which is changing, subject to differing applications and interpretations, and may be inconsistent among countries, or conflict with other rules. We are or may become subject to the terms of contractual obligations related to privacy, data protection and data security. Our obligations may also change or expand as our business grows. The actual or perceived failure by us or third parties related to us to comply with such laws, regulations and obligations could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines and penalties, result in reputational harm, lead to a loss of customers, result in litigation and liability, and otherwise cause a material adverse effect on our business, financial condition and results of operations. See the section titled " Business – Government Regulation – Data Privacy and Security " **in this Annual Report on Form 10- K** for a more detailed description of the laws that may affect our ability to operate. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes.

Our operations may involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition. The rules dealing with U. S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States ~~recently~~ enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1 % excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States ~~. The U. S. Congress is considering legislation that would restore the current deductibility of research and development expenditures; however, we have no assurance that the provision will be repealed or otherwise modified~~ . Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition. We may acquire businesses or products, or form strategic alliances, in the future, and may not realize the benefits of such acquisitions. We may acquire additional businesses or products, form strategic alliances, or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new product candidates or products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. There is no assurance that, following any such acquisition, we will achieve the synergies expected in order to justify the transaction, which could result in a material adverse effect on our business and prospects. We maintain our cash at financial institutions, often in balances that exceed federally- insured limits. The failure of financial institutions could adversely affect our ability to pay our operational expenses or make other payments. Our cash held in non- interest- bearing and interest- bearing accounts exceeds the Federal Deposit Insurance Corporation (" FDIC") insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. For example, the FDIC took control of Silicon Valley Bank on March 10, 2023. The Federal Reserve subsequently announced that account holders would be made whole. However, the FDIC may not make all account holders whole in the event of future bank failures. In addition, even if account holders are ultimately made whole with respect to a future bank failure, account holders' access to their accounts and assets held in their accounts may be substantially delayed. Any material loss that we may experience in the future or inability for a material time period to access our cash and cash equivalents could have an adverse effect on our ability to pay our operational expenses or make other payments, which could adversely affect our business . Pursuant to the terms of the..... best interest as one of our stockholders . The market price of our common stock has historically been volatile, and the market price of our common stock may decline in the future. The market price of our common stock has been, and may continue to be, subject to significant fluctuations. Market prices for securities of early- stage pharmaceutical, biotechnology, and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include: • our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals; • failure of any of our product candidates, if approved, to achieve commercial success; • failure to maintain our existing third- party license and supply agreements; • changes in laws or regulations applicable to our product candidates; • any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices; • adverse regulatory authority decisions; • introduction of new products, services, or technologies by our competitors; • failure to meet or exceed financial and development projections we may provide to the public and the investment community; • the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community; • announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors; • disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies; • additions or departures of key personnel; • significant lawsuits, including patent or stockholder litigation; • if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock; • changes in the market valuations of similar companies; • general market or macroeconomic conditions, including global inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in monetary policy, instability in financial institutions and the prospect of a shutdown of the U. S. federal government; • geopolitical instability **and government actions** , including the ongoing military conflict in Ukraine, conflict ~~in~~ **between** Israel and ~~surrounding areas~~ **various other parties** , ~~and~~ geopolitical tensions ~~in~~ **between** China **and the United States, and the implementation of measures that restrict international trade by the United States, China or other governments** ; • sales of our common stock by us or our stockholders in the future; • trading volume of our common stock; • announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships, or capital commitments; • the introduction of technological innovations or new therapies that compete with our potential products; • changes in the structure of health care payment systems; and • period- to- period fluctuations in our financial results. Moreover, the capital markets in general have experienced substantial volatility that has often been unrelated to the operating performance

of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. In the past, following periods of volatility in the market price of a company' s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation. ~~Series B Certificate of Designation relating to the Series B Preferred Stock.If we are forced to settle a significant amount of the Series B Preferred Stock,it could materially affect our results of operations.~~ Anti- takeover provisions in our charter documents and under Delaware law and the terms of some of our contracts could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.Provisions in our Certificate of Incorporation and Bylaws may delay or prevent an acquisition or a change in management.These provisions include a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue ~~Preferred~~ **preferred** ~~Stock~~ **stock** without stockholder approval.In addition,because we are incorporated in Delaware,we are governed by the provisions of Section 203 of the DGCL,which prohibits stockholders owning in excess of 15 % of our outstanding voting stock from merging or combining with us.Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors,they would apply even if the offer may be considered beneficial by some stockholders.In addition,these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors,which is responsible for appointing the members of management.In addition,the **Certificate of Designation of Preferences,Rights and Limitations of the Series A Preferred Stock (the "** Series A Certificate of Designation **")** relating to our Series A Preferred Stock may delay or prevent a change in control of our company.At any time while at least 30 % of the originally issued Series A Preferred Stock remains issued and outstanding,we may not consummate a Fundamental Transaction (as defined in the Series **A** Certificate of Designation) or any merger or consolidation of the Company with or into another entity or any stock sale to,or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction,without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock.This provision of the Series A Certificate of Designation may make it more difficult for us to enter into any of the aforementioned transactions **as it would require the separate consent of a majority of the holders of the Series A Preferred Stock** .Our Certificate of Incorporation and Bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum certain types of actions and proceedings that may be initiated by our stockholders,and our Bylaws designate the federal courts of the United States as the exclusive forum for actions arising under the Securities Act,each of which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors,officers,employees or agents.Our Certificate of Incorporation and Bylaws provide that,unless we consent in writing to an alternative forum,the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf,any action asserting a claim of breach of a fiduciary duty owed by any of our directors,officers,employees or agents to us or our stockholders,any action asserting a claim arising pursuant to any provision of the DGCL,our Certificate of Incorporation or our Bylaws or any action asserting a claim that is governed by the internal affairs doctrine,in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction.Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our Certificate of Incorporation and Bylaws.Our Bylaws provide that the federal district courts of the United States of America will,to the fullest extent permitted by law,be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (a " Federal Forum Provision ").Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law.While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case,application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.In addition,investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.These choice of forum provisions will not apply to claims brought to enforce a duty or liability created by the Exchange Act.These choice of forum provisions may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors,officers,employees or agents,which may discourage such lawsuits against us and our directors,officers,employees and agents even though an action,if successful,might benefit our stockholders.Stockholders who do bring a claim in the specified courts could face additional litigation costs in pursuing any such claim.The specified courts may also reach different judgments or results than would other courts,including courts where a stockholder considering an action may be located or would otherwise choose to bring the action,and such judgments or results may be more favorable to us than to our stockholders.Alternatively,if a court were to find these provisions of our governance documents inapplicable to,or unenforceable in respect of,one or more of the specified types of actions or proceedings,we may incur additional costs associated with resolving such matters in other jurisdictions,which could have a material adverse effect on our business,financial condition or results of operations. ~~We do~~ We **do not anticipate that we will pay any cash dividends in the foreseeable future. The current expectation is that we will retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain, if any, for the foreseeable future. Future sales of shares by existing stockholders could cause our stock price to decline. If our stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after legal restrictions on resale lapse, the trading price of our common stock could decline. In addition, shares of our common stock that are subject to our outstanding options and restricted stock units will become eligible for sale**

in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act. Future sales and issuances of equity and debt could result in additional dilution to our stockholders. We expect that we will need significant additional capital to fund our current and future operations, including to complete potential clinical trials for our product candidates. To raise capital, we may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. As a result, our stockholders may experience additional dilution, which could cause our stock price to fall. Pursuant to our equity incentive plans, we may grant equity awards and issue additional shares of our common stock to our employees, directors and consultants, and the number of shares of our common stock reserved for future issuance under certain of these plans will be subject to automatic annual increases in accordance with the terms of the plans. To the extent that new options or other stock- based equity awards are granted and, if applicable, exercised, or we issue additional shares of common stock in the future, our stockholders may experience additional dilution, which could cause our stock price to fall. Our principal stockholders own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval. Our directors, officers, 5 % stockholders, and their affiliates currently beneficially own a substantial portion of our outstanding voting stock. Therefore, these stockholders have the ability and may continue to have the ability to influence us through this ownership position. These stockholders may be able to determine some or all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders. We may become exposed to costly and damaging liability claims, either when testing our programs in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims. We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. While we currently have no products that have been approved for commercial sale, the use of our product candidates in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims may be made by participants or patients that use the product candidate or product, healthcare providers, pharmaceutical companies, or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially and adversely affect the market for our products or any prospects for commercialization of our products. Although we currently maintain adequate product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage or that in the future we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired. From time to time we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal information, contractual relations with collaborators and licensors and intellectual property rights. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, could result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows. We continue to incur **significant** costs and demands upon management as a result of complying with the laws and regulations regulating public companies. ~~We~~ **As a public company, and particularly after December 31, 2024, when we ceased to be a " smaller reporting company " and " non- accelerated filer, " and became a " large accelerated filer, " we have and will continue to** incur significant legal, accounting ~~,~~ and other expenses associated with public company reporting requirements **, including** ~~. We also incur~~ costs associated with corporate governance requirements, ~~including~~ **such as** requirements under the Sarbanes- Oxley **Act, the Dodd- Frank Wall Street Reform and Consumer Protection** Act, as well as rules implemented by the SEC and Nasdaq **. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact (in ways we cannot currently anticipate) the manner in which we operate our business. In addition, changing laws, regulations, and standards relating to corporate governance and public disclosure, including those related to climate change and other environmental, social and governance focused disclosures, are creating uncertainty for public companies, increasing legal and financial compliance costs, and making some activities more time- consuming** . These rules and regulations increase our legal and financial compliance costs and make some activities more time- consuming and costly. These rules and regulations may also make it difficult and expensive for us to obtain directors' and officers' liability insurance. **Our management and other personnel will continue to devote a substantial amount of time to these compliance initiatives, and we will continue to incur increased legal and financial compliance costs.** As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers, which may adversely affect investor confidence and could cause our business or stock price to suffer **. In addition, the increased costs may require us to reduce costs in other areas of our business or increase the prices of our product candidates, once commercialized. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We are no longer a " smaller reporting company " within the meaning of the Securities Act and as a result we are or will be subject to certain enhanced disclosure requirements which will require us to incur significant expenses and expend**

time and resources. We are no longer a " smaller reporting company, " as of January 1, 2025 and, as a result, we are or will be required to comply with various disclosure and compliance requirements that did not previously apply, such as the auditor attestation requirements of Section 404 (b) of the Sarbanes- Oxley Act, the requirement that we hold a nonbinding advisory vote on executive compensation and obtain stockholder approval of any golden parachute payments not previously approved, the requirement to provide full and more detailed executive compensation disclosure and the reduction in the amount of time for filing our periodic and annual reports. Compliance with these additional requirements increases our legal and financial compliance costs and causes management and other personnel to divert attention from operational and other business matters to these additional public company reporting requirements. In addition, if we are not able to comply with changing requirements in a timely manner, the market price of our stock could decline and we could be subject to delisting proceedings by the stock exchange on which our common shares are listed, or sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. We are not required to reflect the change in our smaller reporting company status and comply with the increased disclosure obligations until our quarterly report for the quarter ending March 31, 2025, the first quarter in our fiscal year ending December 31, 2025. We will reassess, as of June 30, 2025, whether we continue to qualify as a large accelerated filer for filings beyond the fiscal year ending December 31, 2025 . If equity 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 is influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our common stock could decrease, which in turn could cause our stock price or trading volume to decline. If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may be negatively affected. We are subject to the reporting requirements of the Exchange Act, the Sarbanes- Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes- Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting **. In addition to our management' s report on the effectiveness of our internal controls over financial reporting, our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes- Oxley Act. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation** . We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our annual report filing for that year, as required by Section 404 of the Sarbanes- Oxley Act. This requires that we incur substantial professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner for each period. We may or any subsequent testing by our independent registered public accounting firm may discover 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. **In addition, we may encounter problems or delays in completing the implementation of any requested improvements and receiving a favorable attestation in connection with the attestation provided by our independent registered public accounting firm.** If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act, or if we are unable to maintain proper and effective internal controls, it could result in a material misstatement of our financial statements that would not be prevented or detected on a timely basis, which could require a restatement, cause us to be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, cause investors to lose confidence in our financial information, or cause our stock price to decline. As a public company, we incur significant legal, accounting, insurance, and other expenses, and our management and other personnel have and will need to continue to devote a substantial amount of time to compliance initiatives resulting from operating as a public company. ~~72~~ **We have identified a material weakness in our internal control over financial reporting. If our remediation of the material weaknesses is not effective, or if we experience additional material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial results in a timely manner, and we or our independent registered public accounting firm may conclude that our internal control over financial reporting is not effective, which may adversely affect investor confidence in us and materially and adversely affect our business and operating results. Effective internal controls over financial reporting are necessary for us to provide reliable financial information 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 addition, any testing by us conducted in connection with Section 404 of the Sarbanes- Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may**

require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. 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 consolidated financial statements will not be prevented or detected on a timely basis. As described elsewhere in this Annual Report, we have identified a material weakness in our internal control over financial reporting related to the Company' s accounting and reporting of complex financial instruments, resulting in a determination that the Company' s issued preferred stock is common- like in nature and therefore we should apply the two- class method of calculating net loss per share and include our issued Series A Preferred Stock and Series B Preferred Stock in such calculation for our issued audited consolidated financial statements as of December 31, 2023 and for the year then ended, and our unaudited consolidated financial statements for the quarterly and year- to- date (as applicable) periods ended June 30, 2023, September 30, 2023, March 31, 2024, June 30, 2024 and September 30, 2024 (collectively, the " Affected Periods "). We have implemented measures designed to improve our disclosure controls and procedures and internal control over financial reporting to address the underlying causes of this material weakness, including enhancing the design of controls relevant to the preparation and presentation of financial reporting matters related to net earnings (loss) per share calculations and disclosures to ensure that economic substance beyond the legal form of our capital structure is considered when preparing disclosures related to net earnings (loss) per share. These remediation measures may be time- consuming and costly and there is no assurance that these initiatives will ultimately have the intended effects. While we believe that these efforts will improve our internal control over financial reporting, remediation of the material weaknesses will require validation and testing of the design and operating effectiveness of internal controls over a sustained period of financial reporting cycles. We cannot assure you that these measures will significantly improve or remediate the material weaknesses described above. The material weakness resulted in the restatement of our financial statements for the Affected Periods. As a result of this material weakness, our management has concluded that our disclosure controls and procedures were not effective as of December 31, 2023 and 2024. See Part II, Item 9A. Controls and Procedures included in this Annual Report. While we are taking a number of measures to remediate the material weakness (as described above), if we identify additional material weaknesses, we may be unable to provide required financial information in a timely and reliable manner and we may incorrectly report financial information. Likewise, if our financial statements are not filed on a timely basis, we could be subject to sanctions or investigations by the stock exchange on which our shares of common stock are listed, the SEC or other regulatory authorities. The existence of material weaknesses in internal control over financial reporting could adversely affect our reputation or investor perceptions of us, which could have a negative effect on the trading price of our stock. We can give no assurance that any additional material weaknesses or restatements of financial results will not arise in the future due to a failure to implement and maintain adequate internal control over financial reporting or circumvention of these controls. Even if we are successful in strengthening our controls and procedures, in the future those controls and procedures may not be adequate to prevent or identify irregularities or errors or to facilitate the fair presentation of our financial statements. 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 any measures we may take in the future, will be sufficient to avoid potential future material weaknesses. Our business could be adversely affected by economic downturns, inflation, increases in interest rates, natural disasters, public health crises, political crises, U. S. elections, international or geopolitical events, such as the conflict between Russia and Ukraine, and Israel and various other parties and other conflicts in the region, the implementation of measures that restrict international trade or other macroeconomic conditions, which could have a material and adverse effect on our results of operations and financial condition. The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, higher interest rates, and uncertainty about economic stability. For example, the COVID- 19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. The Federal Reserve has raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, geopolitical uncertainties, international conflicts and government actions, including the ongoing military conflicts between Russia and Ukraine, and Israel and various other parties, including Iran, Hamas and Hezbollah, as well as other conflicts in the region, rising tensions with China and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments, have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more costly, more dilutive, or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs. We may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing sufficient quantities of materials. Any one or a combination of these events could have

a material and adverse effect on our results of operations and financial condition.